

ماجستیر تناسلیه (2)

ANATOMY OF URETHRA (STDS)

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— just print —

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Anatomy of Urethra

♂ Urethra

def : Canal that extend from bladder neck to Ext. urethral Meatus passing through substance of Corpus Spongiosum.

Length : 20 cm.

shape : "S" shaped

Q why predisposed to chronic Inf. ? "urethritis"

d.t. 2 factors < always closed & open only during Micturition
S-shaped

Anatomy

↓ 15 cm.
Ant. Urethra

Bulbous urethra

penile or pendulous urethra

↓ 5 cm.
Post Urethra

prostatic urethra

Membranous urethra

Post urethra (5cm = 3+2)

Prostatic urethra

From neck of bladder
to neck of prostate (passing
through substance of Prostate)

length 3 cm

Ch $\left\{ \begin{array}{l} \text{widest part} \\ \text{Most distensible} \\ \text{part} \end{array} \right.$
has elevation on its
post wall called "

"Verumontanum or Colliculus
seminalis"

Related to 3 opening:

* opening of prostatic
uricle (remnant of
Mullerian duct) \rightarrow open
on Top of C. seminalis
(it's a blind pouch)

Lined by "Transitional
Epithelium"

* 2 openings of
ejaculatory
duct (slit
like) on Both
Sides of

Colliculus \rightarrow "C. seminalis"

Membranous urethra

Extend from
Neck of prostate
passing through

Ext. urethral Sphincter
(w) is enclosed in urogenital
diaphragm.

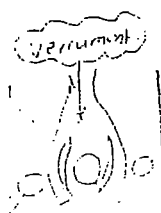
length 2 cm.

Ch $\left\{ \begin{array}{l} \text{Thickest part} \\ \text{Narrow} \\ \text{Muscular} \\ \text{organ (S.K. m} \\ \text{+ smooth m.)} \end{array} \right.$

lined by: Col.
Epithelium

* 2 openings of
prostatic
ducts on either
Side of
Verumontanum
by Depression
= (fossae)
collect.

"prostatic
sinus"





Ant. Urethra

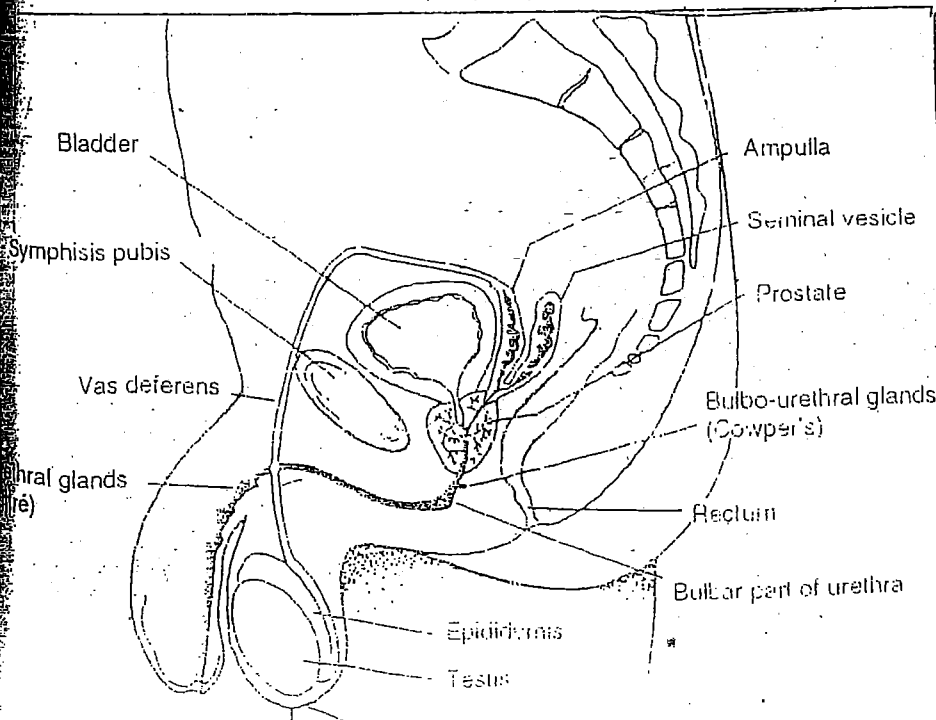
- 15 cm
- Extend From membranous urethra till the end of Ext. Urethral
- All lined by Columnar epith. **EXCEPT** Fossa Navicular (St. Sq. non Keratini Zed).
- 2 parts

Bulbous urethra

Surr. BY bulb of penis & bulbospongiosus Muscle.

Penile = pendulous
= Spongy urethra

start as continuation of bulbous urethra at lowest level of SP. (S. pubis). ends by passing through glands penis to form dilation & Fossa Navicularis - end of Ext. Meatus (Narrow Part).



Glands Related to the Urethra

Gland ducts secretion

Cowpers (Bulbo-urethral glands)

Present at both sides of membr urethra & Their ducts open into bulbar urethra

(E) → Prosemen on Excitation

Littre's (urethral or Periothral glands)

Multiple glands present on submucosa of penile urethra. Open by Multiple ducts on the roof & sides of penile urethra

Openings of the ducts Found on depressions Mucosal Folds called « Lacuna of Morgagni »

Largest one is

Near the Fossa Navicularis & called « Lacuna Magna » on roof of urethra.

Tyson's

proximal to Coronal Sulcus. ducts: open on either side of Frenulum (Fold on under surface of glans penis)

Secrets: Sebaceous secretion (Smegma) w help retract prepuce over the glans (in non-circumcise)

• Paraurethral ducts

Small blind channels that run parallel to terminal Part of urethra & Open near Ext. Meatus

Fossa

Smegma

Accumulate under prepuce → irritate SCC of penis

When Introducing Catheter:

To avoid Impaction in Lacuna of Morgagni

Sphincters of the Urethra

Internal Sphincter

• Ejaculation controlled by
Control the Bladder
"Neck & prostatic"
Urethra above openings
of Ejac. ducts.

Involuntary non striated

(So supplied by autonomic).

Ext. sphincter

• Control the membranous urethra

• Composed of

Striated ms.

(So supplied by somatic)

(Pudendal N.)

Clinically important point: Failure of the prostatic utricle to regress during embryological development may encroach on the surrounding ejaculatory ducts leading to their obstruction and infertility. (EDO).

Female Urethra

• 4cm

• Extend from UB to Ext. urethral Meatus

• Epith. → Proximal: Transitional
distal: str. sq. Epith.

• Glands

① Skenes

Near lower End of Urethra & open into urethral Meatus

② Bartholins

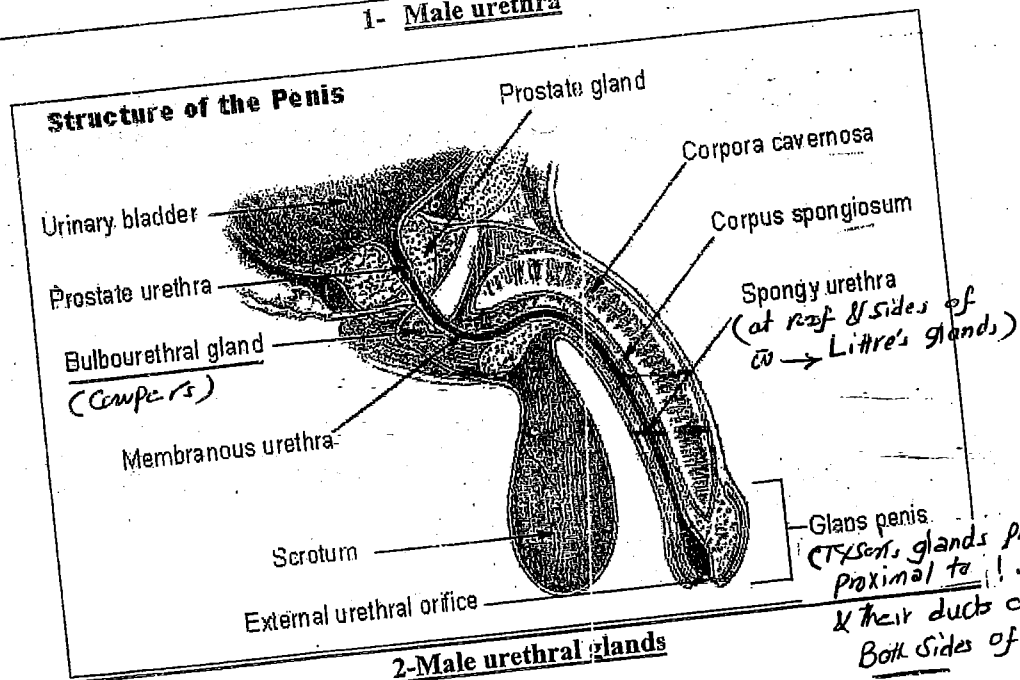
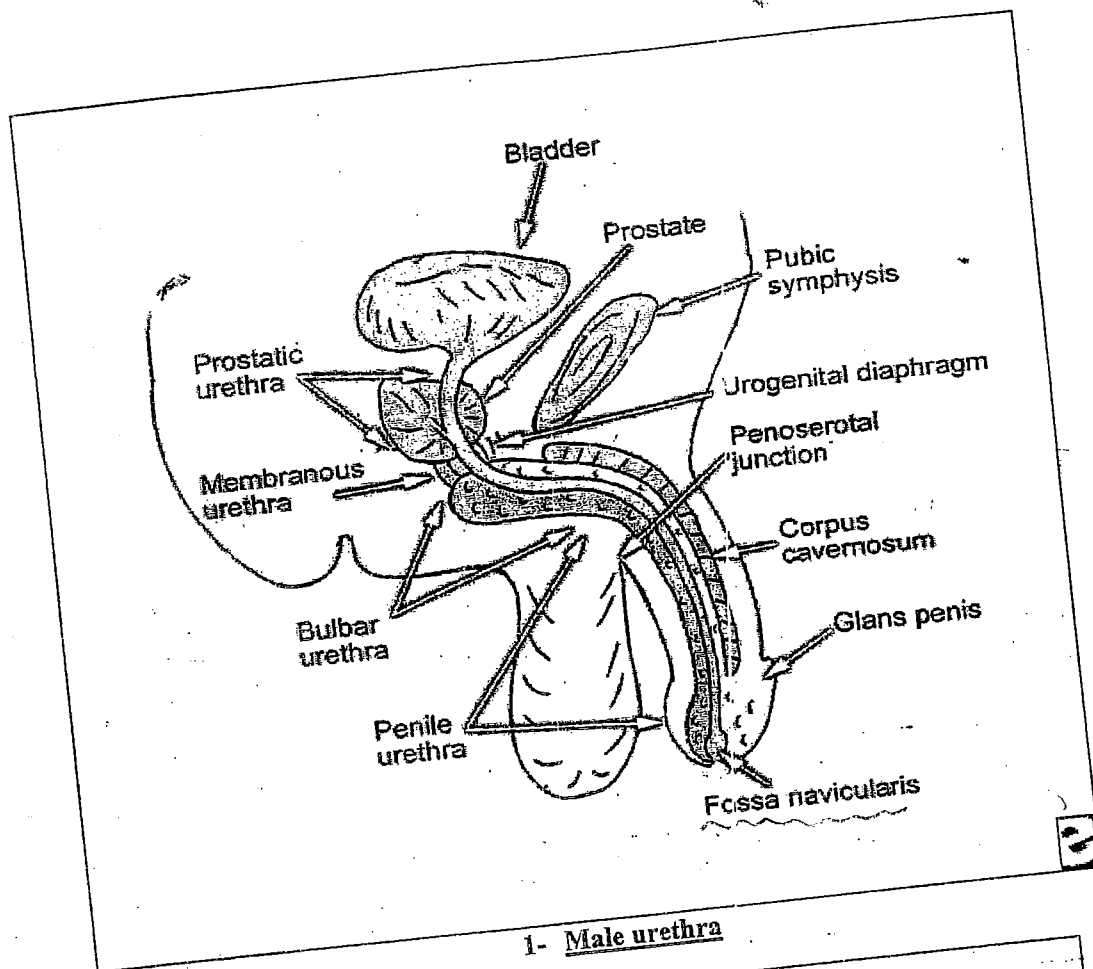
→ Pair of gland.

at ant wall of Vagina around lower end of urethra & drain into it.

present at post. 1/3 of Labia Majora

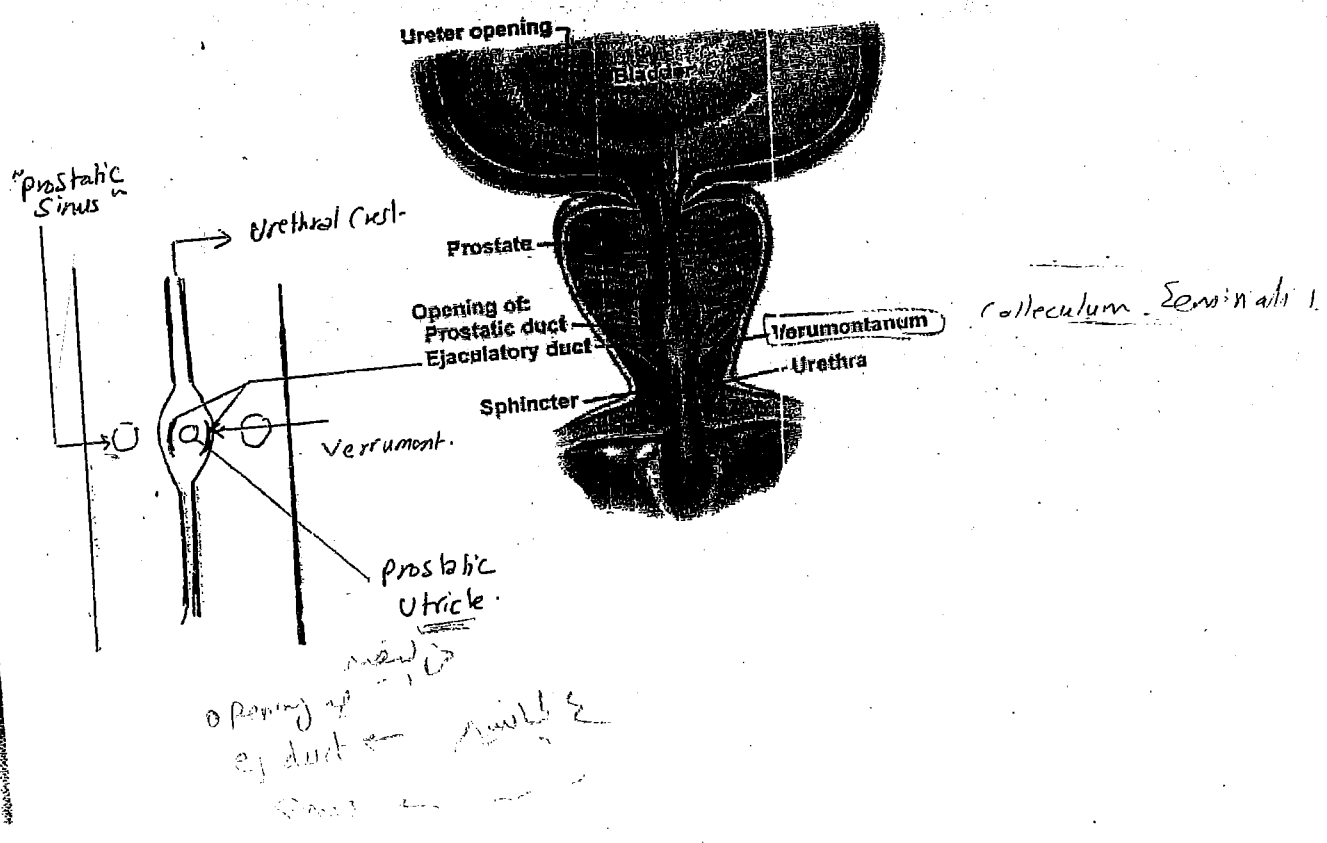
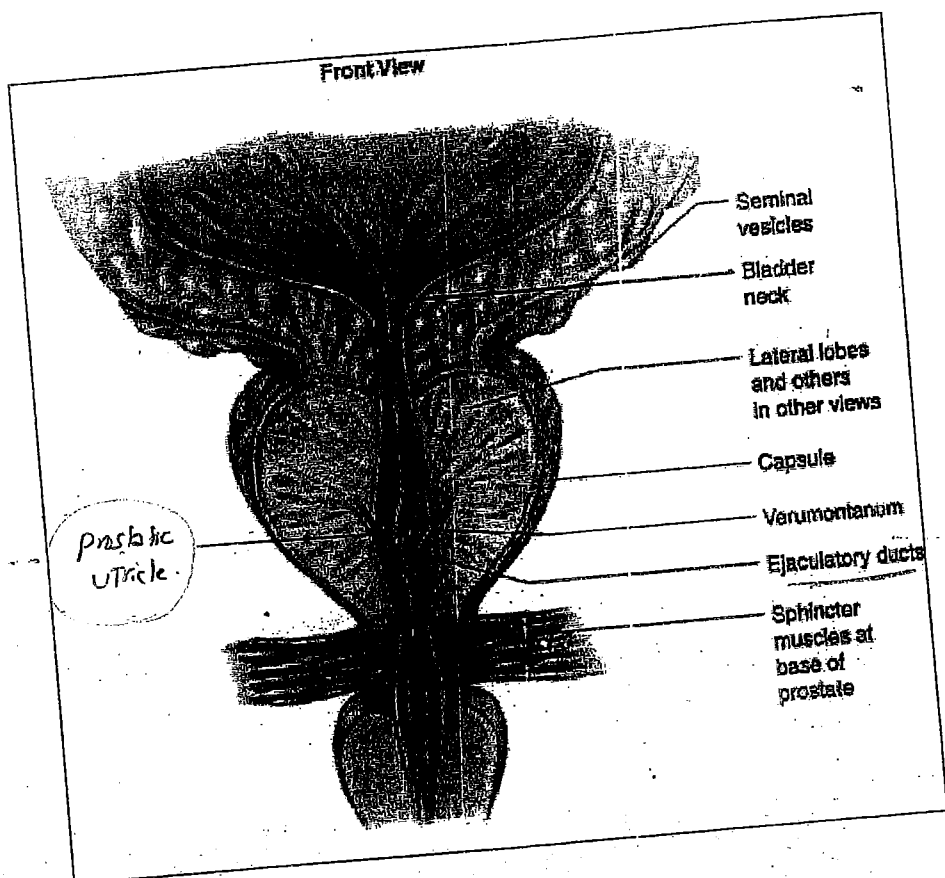
open at inner surface of Labia Minora

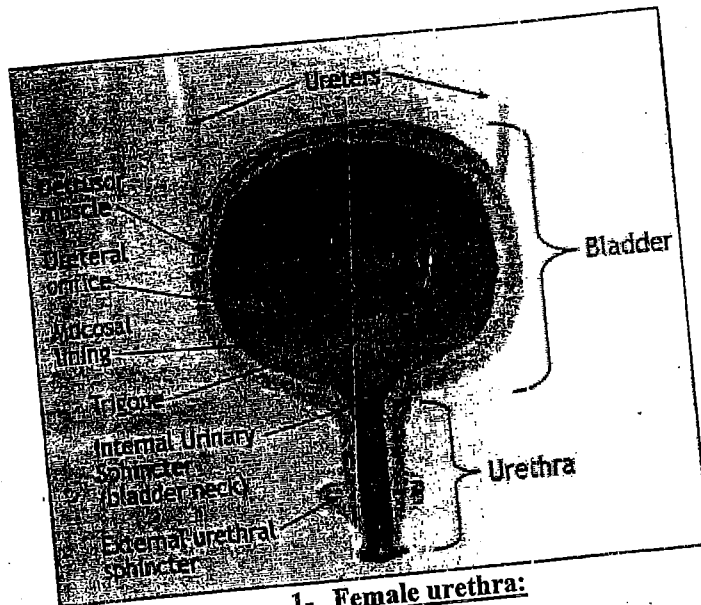
③ Small urethral glands (Similar to Skene's)



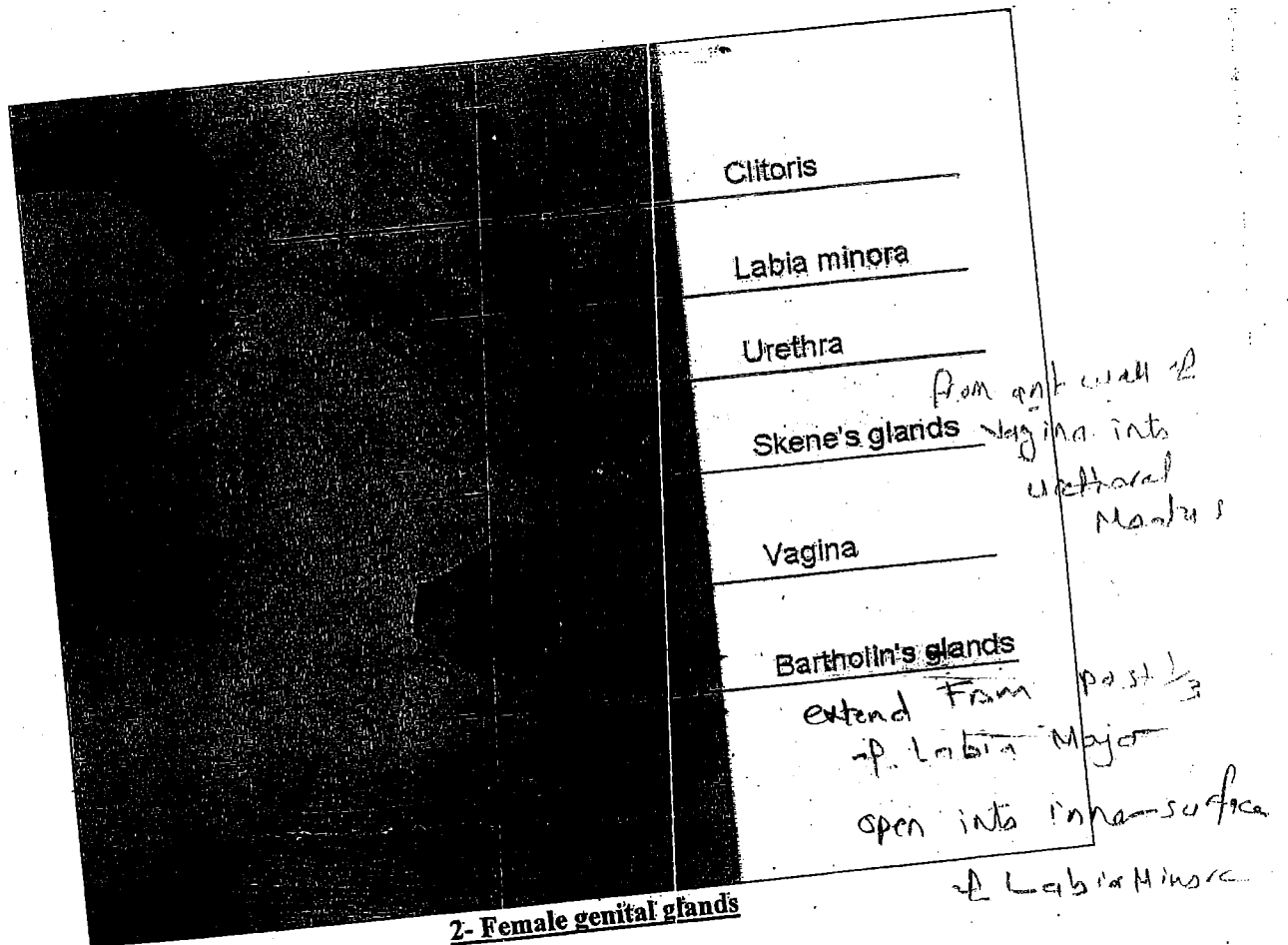
CT secret. glands present proximal to sulcus & their ducts open on both sides of frenulum

dorsal aspect of penis





1- Female urethra:



2- Female genital glands

Gonorrhea (2011)

Def. Acute Infectious dis. of Genitourinary MM caused by NG
Almost exclusively Transmitted Sexually.

Biology of NG

- NG
1. Microbiology
 2. Structure & Virulence
 3. Antibiotic Resist.
 4. Pathogenesis

A- Microbiological characters:

- G-ve, 0.5-1 μ m. low
- Aerobic or Facultative anaerobe (Can grow in presence of air or very low O₂ tension)
- Kidney shaped diplococci
- Multiply intracellular (inside PMNL & epith. cell)
 - NG
 - intracellular in acute inf.
 - extracellular in chronic & very early acute
- None motile, Non capsulated, Non-sporulated
- Can't survive for long time outside the body rapidly destroyed by
 - Dryness
 - Heat
 - Antiseptic
 - Saliva
 (Contain Amino glycosides)

B- Structure and related function:

1. Cell (plasma) membrane (CPM) permeability
2. Peptidoglycan layer \rightarrow strength & osmotic equilibrium.
3. Outer Membrane: (OM)

- (i) Lipopolysaccharides
- endotoxin, ch by:
 - Structural integrity of NG.
 - (Protect against chemical damage)
 - Induct of Immunological Response.

(ii) Lipoproteins

\downarrow

Link bet. peptidoglycan & OM.

(iii) Opa-Protein = opacity associated (Opa)

\downarrow

Adherence to phagocytes & epithelium.

Invasion.

Resistance evasion from Immune System

So infection is possible \leftarrow

- down-regulate of Immune Cell,
- Antigenic Variation

(iv) Porins (Por A & B)

Pores or channels in OM play a role in Virulence.

For chemical molecules

Por A NG has inherent resistance to IgG & Ability to invade the epith (explain their and Bacteremia)

adhesion

✓
periplasmic space: space bet. peptidoglycan & both \angle PM & OM

pili (fimbriae): (grasping - Hooks)
 • Attachment to epit^h.
 • resistance against Neutrophils.

Virulence factors:

1. Opa protein
2. Porens
3. pili
4. Lipopolysaccharides (endotoxins) \rightarrow DGI
5. Produce IgA-protease.

Mechanism of Antibiotic Resistance:

(1) see later (pg. 2)

(2) L-form of NG:

Alteratⁿ in its Morphology (Failed cell wall Synth) may occur spontaneously or by repeated Culture \rightarrow it's insensitive to penicillin only

D. Pathogenesis:

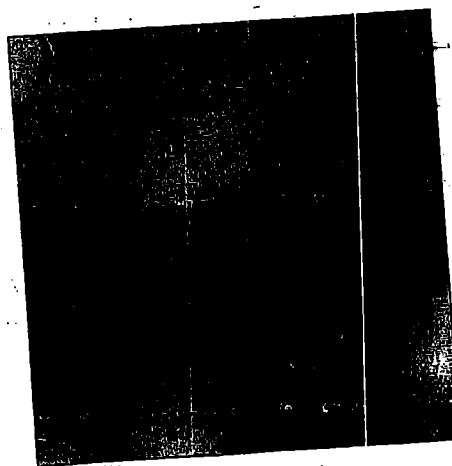
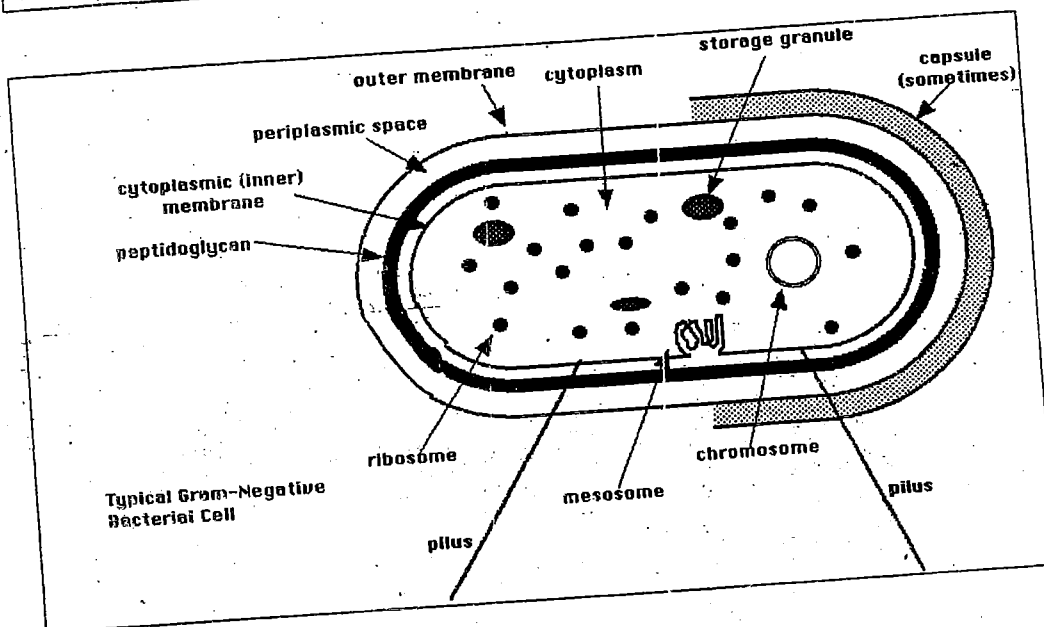
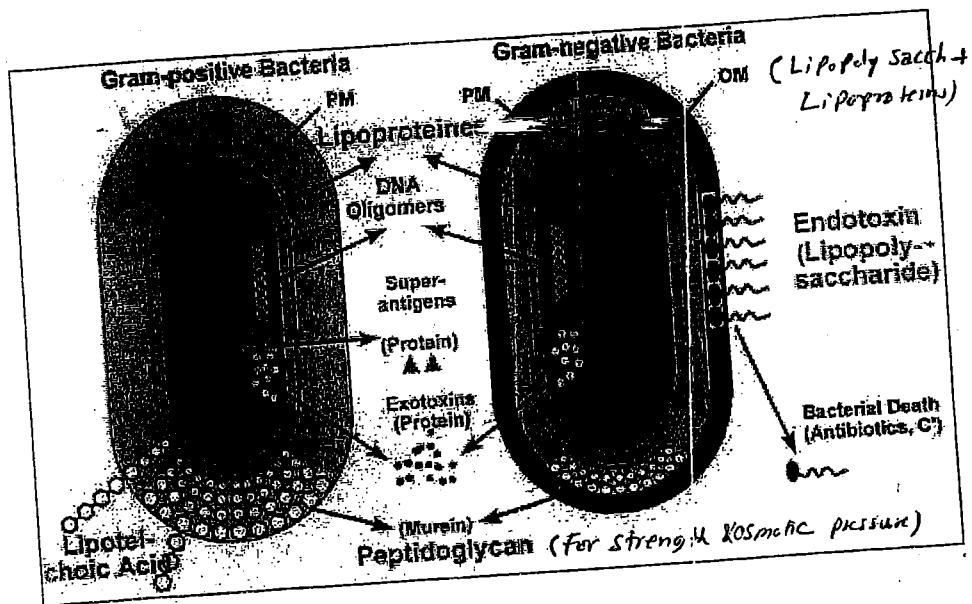
The organism has predilectⁿ to Columnar or cuboidal epithelium so it attacks:
 • in Male: Epididymis, SV, prostate, Cowper's & Littre's
 • in Female: Endocervix, F.T.s; Skene's & Bartholin glands.
 • in Male & Female: Urethra, rectum, oropharynx & Conjunctiva

Gonococci attach to the host mucosal cell (pili and Opa proteins play major roles) and, within 24-48 hours, penetrate through and between cells into the subepithelial space. A typical host response is characterized by invasion with neutrophils, followed by epithelial sloughing, formation of (submucosal) microabscesses, and purulent discharge. If left untreated, macrophage and lymphocyte infiltration replaces the neutrophils. Some gonococcal strains cause an asymptomatic infection, leading to an asymptomatic carrier state in persons of either sex. The ability to grow anaerobically allows gonococci, when mixed with refluxed menstrual blood or attachment to sperm, to secondarily invade lower genital structures (vagina and cervix) and progress to upper genital organs (endometrium, salpinx, ovaries).

Epidemiology

• Inc: 200 million/y.
 • Age: usually Adolescents & Young Adults (20-40)
 • ± children $\left\{ \begin{array}{l} \text{usually: sign of sexual abuse.} \\ \text{May be: non sexual transmission bet. children or} \\ \text{\& from Adults to children or Infected} \\ \text{From} \end{array} \right.$

197 F (1.5:1)



• Stained smear : intracellular DiploCocci.

Mode of Transmission

① Sexual

Heterosexual → urethral inf. @ EndoCx.
 Homosexual → Rectal inf.
 Oral sex → pharynx

② Non sexual

Nematodes via infected birth canal
 Boys & girls → Contaminated Hands & Toilet seats
 Adults (rarely Non sexual)

Risk of Transm. from ♀ → ♂: 20% / episode

Risk of Transmission from ♂ → ♀: 50-70%

CIP

Genital

Extragenital

- proctitis
- oropharyngitis
- conjunctivitis
- Perihepatitis
- DGI

↓
 disseminated gonococcal infection

Adults (Men) Boys

Adults (Women) Girls

Complications

مضاعفات

Local

Systemic

(DGI)

• Perihepatitis

♂ ♀

Adult Male CIP (Gonococcal urethritis)

- IP: 2-7 ds (usually 5)
- CIP: 15% → Asymptomatic → Carrier
- CIP: 85% → Symptomatic:

FAHM (±)

Manifest of Ant. urethritis (Early)

Dysuria

Discharge

Prostate
Purulent
Yellowish-greenish
stains under-clothes
± scanty & mucoid (as NGU).

Manifest of post urethritis (late untreated) (12-14 ds)

Ant. urethritis manifest
Frequency
Urgency
Hematuria (± priapism).

Urinary Meatus → red & Edematous.

L.N. → Enlarged, & Tender.

(+rigor)
↓
columnar epith

Gonorrhea in Adult women (Gonococcal Cervicitis)

IP: ≥ 2 ws (> Men)

CIP: 50% Asymptomatic
50% Symptomatic

Most often & less common

Cervicitis (90%)

Urethritis (80%)

(Endo Cervix)

Commonest presentation ✓

back Pain

Manifestations:

Commonest → low backache
discharge from Ext. OS as is
irritated & itched

Dysuria
Discharge
Frequency
Urgency
Hematuria
Ext. Meatus → red & edem.

in f:
Commonest Site
CX 90%
Urethra 80%
rectum 40%
pharynx 20%

dt Seb-Secretion

indicate Trigonitis.

NB: A normally looking vagina or cervix doesn't Exclude Inf. This because racemose nature of cervical glands → chronicity of infection
 i.e. formation of bluish cysts (Nabothian follicles)
 d.t. Duct obstruction (d.t. creeping & vaginal Epith. over craters ex).

Gonorrhea in Boys:

AET $\left\{ \begin{array}{l} \text{usually Sexual assault} \\ \text{may be: Non sexual contact} \\ \text{in Household} \end{array} \right.$

CIP: dysuria, discharge & proctitis.

As of + proctitis rectum

Gonorrhea in Girls:

AET: as in Boy - (rape).

CIP: vulvo vaginitis + adult like manifs $\left\{ \begin{array}{l} \text{dysuria} \\ \text{discharge} \\ \text{proctitis} \end{array} \right.$

most common presentation

Extra-genital Infection

1. Gono. Conjunctivitis
 may affect

IP: 2-5 ds

Neonates (ophthalmia Neonatorum)

affects the neonates during vaginal delivery (vertical Transmission)
(usually Bilateral)

Adults

d.t. autoinoculation

→ usually unilateral

ophthalmia Neonatorum : usually Bilateral & may → Blindness.

CIP (Both) : → Purulent Conjunctivitis
 → Keratitis.
 → Abscess.
 → Blindness.

2. Oropharyngitis

• d.t oral sex
 • mild pharyngitis. non sp.

3. Proctatits. (Proctitis).

Mode
 ♂ → Homosexuality
 ♀ → Anal sex or local spread from Genococcal endocervicitis (50% Contaminated by endocx. discharge)

NB: 50% of women e Gonorrhoea have proctitis.

• CIP
 + Asymptomatic or Rectal manif:
 [Pain
 [Pruritus
 [Tenesmus
 [discharge
 [Bloody diarrhoea.

DD of proctitis

- Gonorrhoea
- Candida
- δ
- Genital wart
- Chlamydia
- HSV
- non specific.

Complications

Complications of Gonorrhea



Local Complications in ♂

1. Balanoposthitis → Glans & Prepuce
 2. Tysonitis → Swelling at both sides of Frenulum
 3. Lithritis → Swelling at Root & sides of Urethra (Fet by massaging U. against U. sound)
 4. Compensitis → Swelling on both sides of Perineal Raphe → Painful defecation (Fet by Finger in Rectum & Hand on Perineum)
 5. Paraurethritis
Periurethral Abscess
Post. Urethritis
Urethral Stricture → Complicated
 - Prostate → Prostatitis
 - SV → S. Vesiculitis
 - UB → Triginitis
 - Epididymis → Epididymitis
- ulcer Near Frenula
 if abs. & Lympho ngitis & Edema → Bu Head clasp synd
- Painful Swelling at bulb or Fossa navicularis & rarely Fistula.
- C. Spongiosum Infert → Painful & Angulated Erect

Complications of Post Urethritis

1. Prostatitis
2. Seminal Vesiculitis
3. Epididymitis

1. Prostatitis (rare)
 may be acute or chr. usually d.t. non specific inf.
 occurs as complication of post-urethritis
CIP : no discharge

- ✓ Pain: pelvic, suprapubic, penile.
- ✓ Voiding Symp: Dysuria, frequency, urgency, hematuria.
- ✓ Sexual Symp: ED, PE, Priapism & Hemospermia.
- ✓ Infertility ✓
- ✓ Abscess: may open into Rectum → ganglionic proctitis
- ✓ PR Examination ??

2. Seminal Vesiculitis

لتهيج و التهاب
 الغدد seminal

As prostatitis +

Spasmodic pain @ ejac.

Morning Gleet. (irritant)

↓ secretion

3. Epididymitis see infertility.

Local Complications in ♀

Painful tender swelling at base of vagina.
 1/3 of L. Vagina
 difficult sitting & walking

Skinitis: with Paraurethral Cyst or Abscess

Bartholin's: with Bartholine Cyst or Abscess

PID: Salpingitis & Pyosalpinx

chr. pain
 Infertility
 Ectopic preg.

up. abs
 ↓
 commonest
 local
 Complicatn

Parametritis: endometritis

pelvic abscess

peritonitis

proctitis: → ± Asympt. or rectal manif.

Tubal Obst

Tubo-ovarian abscess.

Systemic Complications

A

Perihepatitis...

→ spread of inf. to peritoneum

(Fitz Hugh-Curtis Synd)

AET: spread of inf. By:
 In. ♂ & ♀ → Blood
 In ♀ only → Through the Tubes & their continuation in the peritoneum.

Violin-string
 Complicatn

(adhesion bet
 liver &
 diaphragm)

CIP ① Acute onset of:

Fever

Nausea

Pain

Rt Hypochondriac

↑ by cough

referred to shoulders

② Complications

Gono-Cocemia
Arthritis -
Dermatitis
Synd.

Disseminated Gonococcal Infection

(DGI)

Disseminated

Incid: 0.5-1% (d.t. Blood spread → Capillary embolization by cocci & release of Toxins)

Risk factors:

① Menstruation & pregnancy (d.t. changed pH → ↑ Cervical shedding ↓ Bact. enzy in Mucosa)

② Hypo complement-emia (C5, 6, 7 & 8)

③ A/H type of organism.

④ Resistance To bactericidal IgM (d.t. Antigenic Variation in their Poly saccharide Endotoxins)

Antiplas Antibody

⑥ pharyngeal inf.

High incid. of Asympt. (most) disseminated

CIP

2 forms:

Mild form

Fever (< 39°C)

Arthritis

Rash

Maculopapular, Vesicular, Bullous, Pustular, Ery or Necrotic

Polyarthralgia

Tenderness, Limitation, Erythema, + Purulent

Large joints

Severe form

Hepatitis →

Carditis → Tach. & Murm

Encephalitis → meningism

Osteomyelitis

Myositis → abscess

Tenosynovitis → at hand

Iridocyclitis (Allergic re)

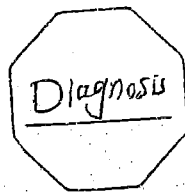
at distal Extremities e.g. Palm & Anus

usually spare:

Face, scalp & mouth.

NB Eye affects

Conjunctivitis, Trichocilia



→ Urinalysis

1. Glass Tests

2. Stained smear
3. Culture & Sensitivity
4. Biochemical Reactions
5. Antigen detection
6. Gene detection

7. Others

1. urine analysis & glass Tests:

2 glass Test

Micturatur in 2 glasses:

If there is:

- Ant. urethritis:
 - 1st specimen → HAZY
 - 2nd " → clear
- Post urethritis 2 glasses
- or specimens are HAZY

3 glass Test

3 glasses: contain

1st → Irrigated ant urethra.

2nd → contain the few amount passed by urinate

3rd → remainder of urine passed by urinate

↓ If:

Turbidity in

- 1st glass → ant urethra
- 2nd " → Post
- 3rd " → Trigo (Blad Inf)

2

A. Urine

3. Exu

• MEN! →

pharynx inf

Pharynx - J
Ekin Inf

طالبا

DGI ← Josh
CSF
Blood

10

② Swab

10

(Not Co.)

③ 2 hrs

Th

1998, 1999, 2000, 2001, 2002, 2003, 2004, 2005, 2006, 2007, 2008, 2009, 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2017, 2018, 2019, 2020, 2021, 2022, 2023, 2024, 2025, 2026, 2027, 2028, 2029, 2030, 2031, 2032, 2033, 2034, 2035, 2036, 2037, 2038, 2039, 2040, 2041, 2042, 2043, 2044, 2045, 2046, 2047, 2048, 2049, 2050, 2051, 2052, 2053, 2054, 2055, 2056, 2057, 2058, 2059, 2060, 2061, 2062, 2063, 2064, 2065, 2066, 2067, 2068, 2069, 2070, 2071, 2072, 2073, 2074, 2075, 2076, 2077, 2078, 2079, 2080, 2081, 2082, 2083, 2084, 2085, 2086, 2087, 2088, 2089, 2090, 2091, 2092, 2093, 2094, 2095, 2096, 2097, 2098, 2099, 2100, 2101, 2102, 2103, 2104, 2105, 2106, 2107, 2108, 2109, 2110, 2111, 2112, 2113, 2114, 2115, 2116, 2117, 2118, 2119, 2120, 2121, 2122, 2123, 2124, 2125, 2126, 2127, 2128, 2129, 2130, 2131, 2132, 2133, 2134, 2135, 2136, 2137, 2138, 2139, 2140, 2141, 2142, 2143, 2144, 2145, 2146, 2147, 2148, 2149, 2150, 2151, 2152, 2153, 2154, 2155, 2156, 2157, 2158, 2159, 2160, 2161, 2162, 2163, 2164, 2165, 2166, 2167, 2168, 2169, 2170, 2171, 2172, 2173, 2174, 2175, 2176, 2177, 2178, 2179, 2180, 2181, 2182, 2183, 2184, 2185, 2186, 2187, 2188, 2189, 2190, 2191, 2192, 2193, 2194, 2195, 2196, 2197, 2198, 2199, 2200, 2201, 2202, 2203, 2204, 2205, 2206, 2207, 2208, 2209, 2210, 2211, 2212, 2213, 2214, 2215, 2216, 2217, 2218, 2219, 2220, 2221, 2222, 2223, 2224, 2225, 2226, 2227, 2228, 2229, 2230, 2231, 2232, 2233, 2234, 2235, 2236, 2237, 2238, 2239, 2240, 2241, 2242, 2243, 2244, 2245, 2246, 2247, 2248, 2249, 2250, 2251, 2252, 2253, 2254, 2255, 2256, 2257, 2258, 2259, 2260, 2261, 2262, 2263, 2264, 2265, 2266, 2267, 2268, 2269, 2270, 2271, 2272, 2273, 2274, 2275, 2276, 2277, 2278, 2279, 2280, 2281, 2282, 2283, 2284, 2285, 2286, 2287, 2288, 2289, 2290, 2291, 2292, 2293, 2294, 2295, 2296, 2297, 2298, 2299, 2300, 2301, 2302, 2303, 2304, 2305, 2306, 2307, 2308, 2309, 2310, 2311, 2312, 2313, 2314, 2315, 2316, 2317, 2318, 2319, 2320, 2321, 2322, 2323, 2324, 2325, 2326, 2327, 2328, 2329, 2330, 2331, 2332, 2333, 2334, 2335, 2336, 2337, 2338, 2339, 2340, 2341, 2342, 2343, 2344, 2345, 2346, 2347, 2348, 2349, 2350, 2351, 2352, 2353, 2354, 2355, 2356, 2357, 2358, 2359, 2360, 2361, 2362, 2363, 2364, 2365, 2366, 2367, 2368, 2369, 2370, 2371, 2372, 2373, 2374, 2375, 2376, 2377, 2378, 2379, 2380, 2381, 2382, 2383, 2384, 2385, 2386, 2387, 2388, 2389, 2390, 2391, 2392, 2393, 2394, 2395, 2396, 2397, 2398, 2399, 2400, 2401, 2402, 2403, 2404, 2405, 2406, 2407, 2408, 2409, 2410, 2411, 2412, 2413, 2414, 2415, 2416, 2417, 2418, 2419, 2420, 2421, 2422, 2423, 2424, 2425, 2426, 2427, 2428, 2429, 2430, 2431, 2432, 2433, 2434, 2435, 2436, 2437, 2438, 2439, 2440, 2441, 2442, 2443, 2444, 2445, 2446, 2447, 2448, 2449, 2450, 2451, 2452, 2453, 2454, 2455, 2456, 2457, 2458, 2459, 2460, 2461, 2462, 2463, 2464, 2465, 2466, 2467, 2468, 2469, 2470, 2471, 2472, 2473, 2474, 2475, 2476, 2477, 2478, 2479, 2480, 2481, 2482, 2483, 2484, 2485, 2486, 2487, 2488, 2489, 2490, 2491, 2492, 2493, 2494, 2495, 2496, 2497, 2498, 2499, 2500, 2501, 2502, 2503, 2504, 2505, 2506, 2507, 2508, 2509, 2510, 2511, 2512, 2513, 2514, 2515, 2516, 2517, 2518, 2519, 2520, 2521, 2522, 2523, 2524, 2525, 2526, 2527, 2528, 2529, 2530, 2531, 2532, 2533, 2534, 2535, 2536, 2537, 2538, 2539, 2540, 2541, 2542, 2543, 2544, 2545, 2546, 2547, 2548, 2549, 2550, 2551, 2552, 2553, 2554, 2555, 2556, 2557, 2558, 2559, 2560, 2561, 2562, 2563, 2564, 2565, 2566, 2567, 2568, 2569, 2570, 2571, 2572, 2573, 2574, 2575, 2576, 2577, 2578, 2579, 2580, 2581, 2582, 2583, 2584, 2585, 2586, 2587, 2588, 2589, 2590, 2591, 2592, 2593, 2594, 2595, 2596, 2597, 2598, 2599, 2600, 2601, 2602, 2603, 2604, 2605, 2606, 2607, 2608, 2609, 2610, 2611, 2612, 2613, 2614, 2615, 2616, 2617, 2618, 2619, 2620, 2621, 2622, 2623, 2624, 2625, 2626, 2627, 2628, 2629, 2630, 2631, 2632, 2633, 2634, 2635, 2636, 2637, 2638, 2639, 2640, 2641, 2642, 2643, 2644, 2645, 2646, 2647, 2648, 2649, 2650, 2651, 2652, 2653, 2654, 2655, 2656, 2657, 2658, 2659, 2660, 2661, 2662, 2663, 2664, 2665, 2666, 2667, 2668, 2669, 2670, 2671, 2672, 2673, 2674, 2675, 2676, 2677, 2678, 2679, 26

HPF \uparrow

Direct
MIC. ex

[illegible]

Not used
in - prognosis

أَفْعَالٌ

ram - ve, Kig

Intracellular

inside PMN

Rapport

① don't show
staining f

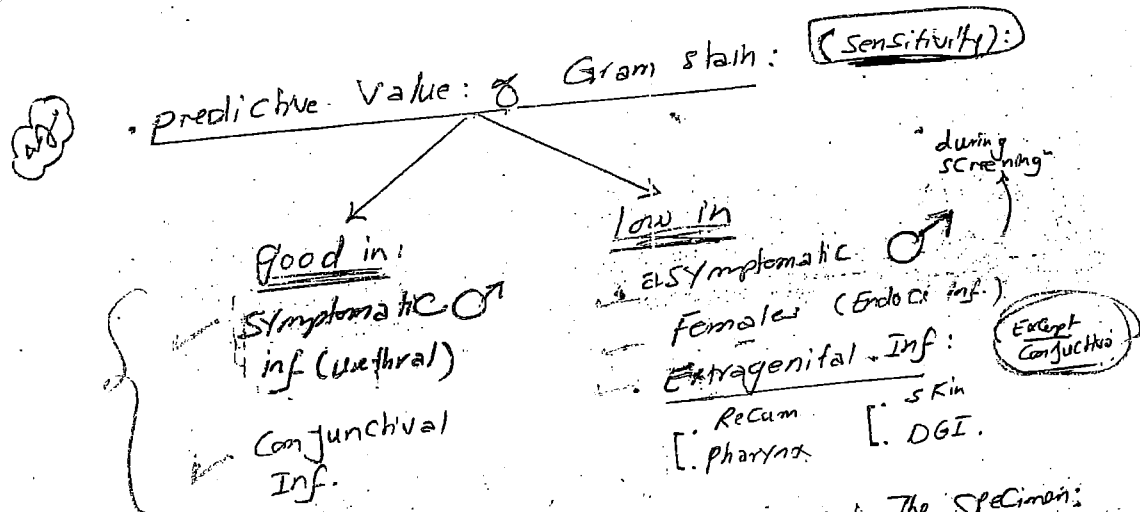
as Gra
wood

(2) Need
Condition
Factor

Sensitive
But

Not spec

1



DD of Gram - ve stain organisms in the specimen:

- ①. Denaturated staph, lost their stain & become G-ve.
- ②. Short cocciform bacteria: in ♀ genitalia. (E. coli)
- ③. Moraxella & Actino bacter group.

Technique of Gram Stain:

Stain 1%

Crystal Violet

↓ rinse w Water (after 20 sec)

Add Gram's Iodine

↓ rinse w water (after 20 sec)

Remove the stain.

↓ rinse w water

Counter stain w Neutral red

↓
Examined.

3.

Culture

(Most Accurate For
Sensitivity 90% &
Specificity 95%)

A. Indications:

1. Asymptomatic Males
2. Females (Endo CR Inf.)
3. Extragenital Inf: (Except Conjunctiva):
Rectum • Skin
Pharynx • DGI

Gram stain
→

4. doubtful diagnosis.
5. Medico legal Conditions (Rape or Abuse)

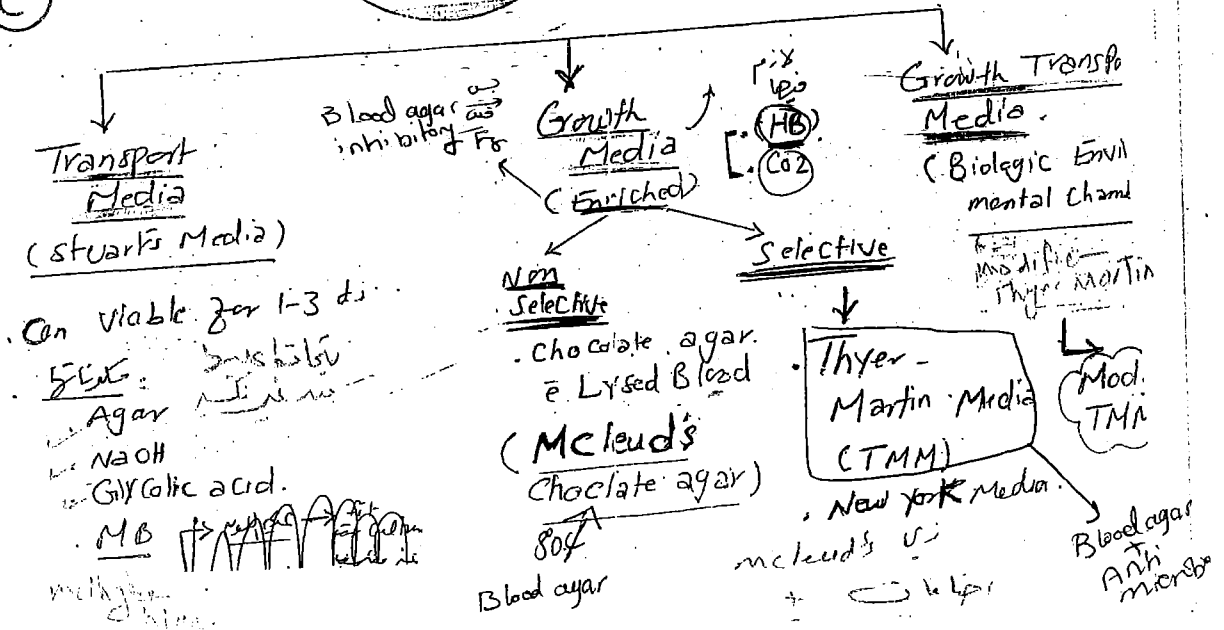
B. Sensitivity:

Source of the sample	Diagnostic sensitivity	
	Gram stain	Culture
① Symptomatic males	98%	98%
② Females and asymptomatic males	95%	95%
③ Conjunctiva	Not recommended	25-75%
④ Pharynx, rectum and blood in disseminated infection.		

Extragenital

C

Media (agars)



NB: ^{5/2/23} Enriched Selective media ±

① Antibiotic Containing (Thyer Martin):

Trimethoprim {
 Vancomycin → -- G+ve
 Nystatin → -- Yeast
 TMP → -- Proteus
 Colistimethate → -- G-ve.
 colistimethate

② Selective New York Media

The following needed for culture.

CO₂: 5%
 Moisture: 70%
 Temp: 36°C

↓ 48 hrs (لا تنتظر نتيجة لزراعة واحدة)
 مع ج ك طول ✓

Colonies {
 glistening
 Soft
 Rounded (0.5 mm - 2 cm)

↓ 4 Types

① Type I & II {
 Small
 Pigmented → Pathogenic
 = Pili (Fimbriae)

② Type III & IV {
 large
 unpigmented → Non pathogenic
 No pili

Antibiotic sensitivity (In one study (2007) on 60 strains isolated from 62 pts)

all strains susceptible to {
 Cefixime
 Ceftriaxone
 Azithromycin
 Spectinomycin.

Some strains are resistant to {
 Cipro.
 Penicillin
 Tetracycline

4. Biochemical & Nutritional Tests

Oxidase Reaction

- Non Specific (type in *Pseudomonas* & *Hemophilus*)
- Detect Gonococcal Colonies in Mixed Cultures

Add oxidase Reagent
(4-methyl para phenylene)

Gonococcal Colonies: Turn pink-purple.

Fermentation Reaction

Glucose, Maltose, Lactose, Sucrose added to the culture

+ Indicator
(8 Acid production)
(Fermentation: Red to yellow)

Used to: detect *N. Gonorrhoea* in areas contaminated & other strains e.g. Rectum & Pharynx.

Auxotyping (AUX = growth)

Classification system for detected 8 Nutritional requirements of *N. Gonorrhoea*.

it was found that *Neisseria G.* that depend on AUX in their nutrition may be as follows:

- ① urethritis.
- ② disseminated Inf.
- ③ Penicillin Sensitivity

Gonococci doesn't ferment maltose
Neisseria meningitidis → ferment maltose

<i>N. gonorrhoeae</i>	→ Glucose only.
<i>N. meningitidis</i>	→ Glucose + Maltose.
<i>N. lactamica</i>	→ Glucose + Maltose + Lactose.
<i>N. pharyngis sicca</i>	→ Glucose + Maltose + Sucrose
<i>N. catarrhalis</i>	→ No fermentation.

NB: Auxotyping was done by Testing the strains for their requirements for: (8)

- Arginine
- Proline
- Uracil
- Hypoxanthine
- Serine
- Iso Coline
- Cysteine
- Cytidine.

So N. G →

Classified into 8 auxo-types

Peri →

non requiring
NR 40%

arginine requiring
proline requiring

5 Antigen detection

used to detect gonorrheal Ags in Fluids collected from penis or Cervix.

done by: ELISA

disadv: less accurate than culture.

6 Gene detection (Biological detection)

Indications:

تفريق بين الازواج
في المختبر
في العيادة
في المختبر
في العيادة

5 Culture in medical legal conditions.

1. Specimen transported over long period.
2. Suboptimum culture conditions.
3. Concomitant chlamydial diagnosis (أحياناً)
4. done on Body Fluids. So useful in conditions in which there is difficulty in obtaining mucosal swab (children)

Adv: sensitive & specific as culture.

disadv: 1. don't provide Antibiotic susceptibility (as) culture.

2. less accurate in presence of Blood or Menstr.
3. Needs longer times.

Types:

Nucleic Acid Hybridization Test (DNA probe test)

Special probe used to detect gonorrheal DNA in the specimen.

NB: Not Accurate in Throat Sample.

Nucleic acid Amplification Tests (NAATs)

done by: PCR or LCR

NB: Rapid > culture
don't require viable organism.

non culture test

7. Other Tests.

A. Serological Tests e.g. ELISA, RIA & Coagulation test.

Value → Carrier detection among high risk groups.

disadv → high antigenic protein varieties.

Classif. → gonococci are classified Acc. to Antigenic variations of the proteins on the outer cell memb. into:

3 Serotypes:

① WI

② WII

③ WIII

Then subclassification may be done using Monoclonal Antibodies.

• Coagulation test

Rapid slide test

slaph coated
antigonal Abs
+
gonococcal suspension

↓
Agglutination
(granular)

B.

Other Invs for detection of

Other STDs e.g. HIV, chlamydia ✓
↓
(associate 50% of Gonorrhea).

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Staph coated +
antigenococcal Abs
+
Gonococcal suspension

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Agglutination
(granular)

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↓
(associate 50% of Gonorrhea).

Treatment of Gonorrhea

① General Measures:

- No intercourse for 2-4 wks.
- Both Partners should be Treated (جماع و آخره را به هم) at the same time.

avoid $\left\{ \begin{array}{l} Alcohol \\ Exertion \\ Self exam. \\ local anti-sphincter \end{array} \right\} \rightarrow \text{may cause "Traumatic urethritis"}$
 $\rightarrow \text{may cause chemical urethritis}$

② Antibiotic Therapy:

- A. Recent IT: According to CDC 2010
- B. Old IT: Not recommended nowadays due to resistance

غیر موجود

Ideal Antibiotic should be:

- Effective.
- Low cost.
- No $\left\{ \begin{array}{l} Allergy \\ Toxicity \\ pregnancy \\ complications \end{array} \right\}$

Effective against $\left\{ \begin{array}{l} chlamydia \\ \text{etc.} \end{array} \right\} \rightarrow \text{"So not masking it"}$

نوع کرمین
Gonorr. (ایس ال ای)

IT of Chlamydia: (ass. gonorrhea in ~ 50%)

Azithromycin (1gr) \rightarrow single dose

or Doxycycline (100) $\rightarrow (1 \times 2 \times 7)$

Erythromycin

Ceftriaxone (IM)

Antibiotic (آنتی بیوتیک)
ج. لا

+ Flagyl for trichomonus

1-2.4gr

A CDC Updated recommended treatment regimens for gonococcal infections and associated conditions - United States, 2010

1. uncomplicated Gonorrhoeae of Urethra, Cx or Rectum:

Recommended Regimen

أنتين سيفترايكون 500. ٢٠٠ (فقط)

Cefixime 400 (أو) جرعة واحدة

(Ximacef 400 Caps)

Alternative Regimen

Spectinomycin → ٢٠٠ ٢٠٠

or Cefuroxime (1g single)

or AZithro (2g single) ٢

2

uncomplicated pharyngeal Inf. → Ceftriaxone 250 mg IM (Single) + AZithro (1g Single) or Doxy 7d

3

Gonococcal Epididymitis → 250mg Ceftriaxone IM (Single) + (Doxy) 100 x 2 x 10

4

Gonococcal Conjunctivitis (adults) : Ceftriaxone 1g single inf + Saline irrigat + Antibiotic Eye oint.

uncomplicated

5

DGI

مرحلة

[Hospitalization]

[Skin rash, arthralgia, anuria]

IV

1. المرحلة الأولى : IV Ceftriaxone 1g / 24 hrs until clinical improvement & continue for 24-48 hrs after that.

400 x 2 x 7d

2. المرحلة الثانية : "oral"

Cefixime 400 mg (أو) ٢٠٠ ٢٠٠

6

Complicated DGI (Endocarditis or Meningitis)

Ceftriaxone 1-2g IV

Meningitis : ٢٠٠ ٢٠٠
Endo-cardh : ٢٠٠ ٢٠٠ (1-2g bid)

7. Ophthalmia Neonatorum:

A. Prophylactic: 0.5% Erythromycin oint; in Both eyes
 Single application.
 عارضة عينية أو حادة
 بعد الولادة مباشرة.

Tetracycline
 Synercid
 Nitrofurantoin
 (لا تستخدموا)

B. Curative IT: 25-50 mg/kg (Not > 125 mg)
 Ceftriaxone Single inj.

No need for
 Topical

9. For children inf:

Wt > 45 → as adults

Wt < 45 → adjust the dose of
 ceftriaxone [50 mg/kg]

علاج

1. (1) Gonorrhea in pregnant علاج

(2) علاج لامرأة الحامل من Gonorrhea

علاجها بالمضاد الحيوي

1. Chlamydia

2. Trichomonas

ازاي تعرف اذا كانت المرأة مصابة بعدوى، علاج

How To avoid Masking 8 & by IT??

ما هو أفضل مضاد حيوي Antibiotic في علاج

Indications of hospitalization:

- initial treatment of (DGI), purulent joint infections, meningitis, and endocarditis.
- initial treatment of PID cases in the presence of the following factors:
 - Pregnancy
 - Failure of outpatient treatment
 - Tuboovarian abscess
 - Severe symptoms (eg, severe pain, high fever, persistent nausea and vomiting)
 - Immunodeficiency
 - Abdominal peritonitis or perihepatitis
 - Uncertain diagnoses, with any possibility of ectopic pregnancy or appendicitis masquerading as PID
 - Uncomplicated urethritis, cervicitis, or rectal or pharyngeal infection in adults

Mechanism of Antibiotic Resistance

In Gonorrhea

Chromosomally Mediated

- Mech. Chromosomal mutations in their genes \rightarrow \downarrow permeability of Gonococcal memb to the antibiotics.

Leads to: Partial or low resistance.
To All Antibiotics.

Overcome: \uparrow dose of " it by

Extra Chromosomally Mediated (Plasmid)

- Mech. plasmids are an Extra chromosomal DNA Particles that can \rightarrow β -lactamase (penicillinase enz)

لبنين (lactam ring)

Leads to: Complete or High Total resistance to some Antibiotics.

Overcome: Not by \uparrow the dose but by changing the antibiotic (penicillamine resistant).

دع

Causes of Ht Failure:

- Reinfection (عدوى متكررة)
- Antibiotic Resistance
- Post gonococcal urethritis (PGU) = d.t untreated chlamydia
- Associated Trichomonas (أش)

دع

Follow up of gonorrhea (Follow up of Ht = Tests for cure)

- * At:
 - 2 days \rightarrow stop of discharge (sign of successful Ht)
 - 1 w \rightarrow Test for gonorrhea & chlamydia (تأكد من الشفاء)
 - 2 ws \rightarrow Examine for complications (prostatovesiculitis)
 - 3 ms \rightarrow Test for β & HIV.

* Gonococcal proctitis: Seen after 1w for rectal swab & culture (should be -ve).

فوق نوع نشر

أغ What is Gonococcal Carriers

• affect 5-10% of Males Infected
with gonorrhea « Asymptomatic Inf »

• More common in ♀ (50%)

• Diagnosis: if little Mucopus ← can be "milked" From meatus & shreds
are present in urine → the condition
more liable to complications.

• Asympt. Cases usually d.t. AUH

Arginine
Ureacilase
Hypoxanthine

why Inf. doesn't give life lasting

Immunity??

① Short IP (short Antigenic Time Exposure)

② Weak Immunity (OPA protein)

③ Heterogenous Antigenicity of organism: ✓

high variety

d.t. 3 different OM proteins (PII) so 3 different
strains are recognized during reproduction
These strains GPII constantly changed.

④ Early antibiotic Ht → Constat & (local) Immunity

⑤ Trichomonas vaginalis: may act as phagocyte
To N. Gonorrhoea that can live inside
Trichomonad & undergo division & despite
anti gonococcal Ht → relapse
So Trichomonas may serve as reservoir for
gonococci in cases of mixed Inf. &
cause relapse.

II Chlamydia Trachomatis (Human)

There are 15 Serotypes (BY MIF)

affecting 2 Systems

Eye
(A, B, B₁ & C)

↓
Trachoma

Genital System

Mucosal

(Non Invasive)
(Serotypes D-K)

↓ non gonococcal urethritis

① NGU

② Reiter's Synd.

③ Others (2-3)

Lymphatics

(Invasive)

① L₁ ② L₂ & ③ L₃

↓
LGV

lymphogranuloma venereum

Taxonomy

① Species

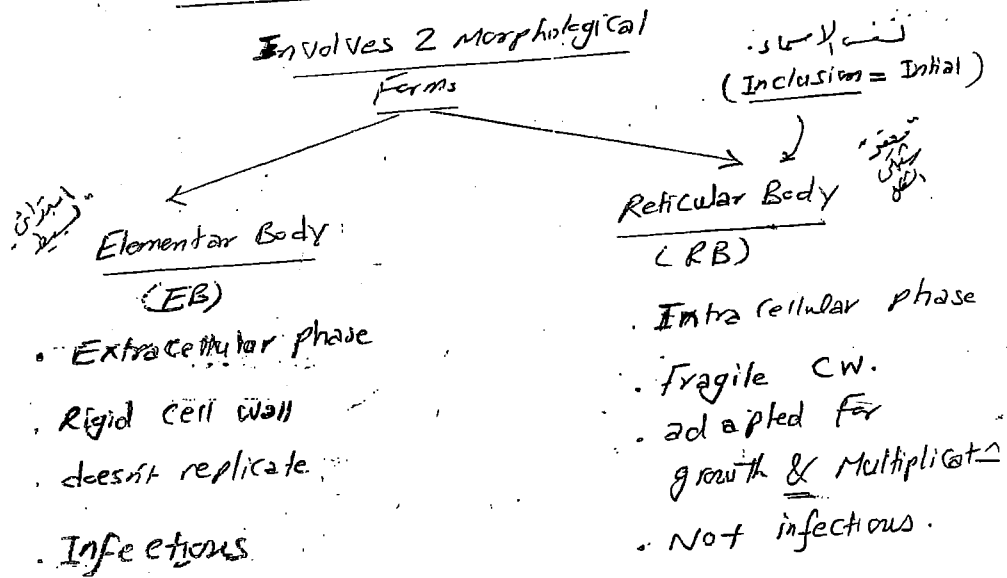
② Serovars (based on OCM-proteins)
(A - L₃)

③ Biovars: LGV ass
vs Non LGV ass.

Life Cycle:

- requires 36-48 hrs.
- has predilection to Columnar Epith but LGV strains can infect St-Sq. Epith.

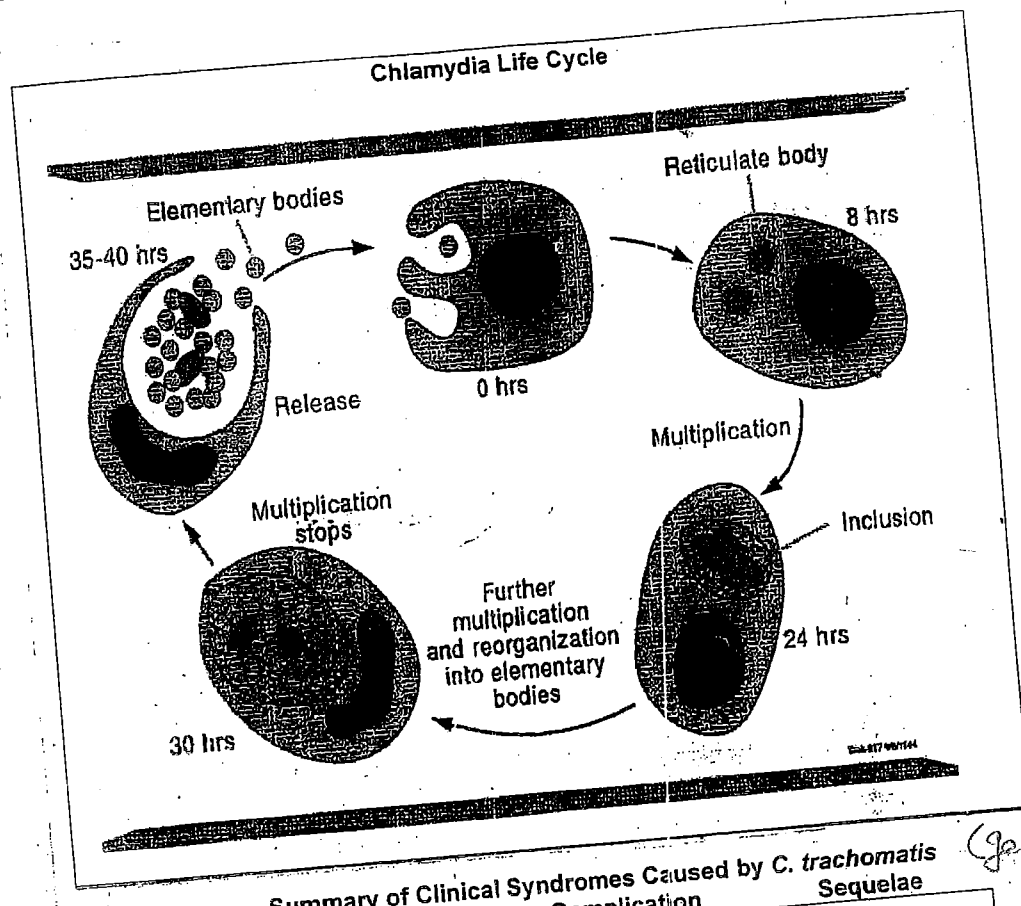
• Life Cycle of Chlamydia



• Pathophysiology:

- EB attaches To the Cp. Epithelium → phagocytosed
- Inside phagocytic vacuole → Failed phagolysosomal destruction (No known AET.)
- EB: Inside The phagocytic vacuole $\xrightarrow{\text{تبعز}}$ RB → grow & multiply by binary fission.
- RB Then → multiply & fill the cytoplasm (Inclusion Body)
- Then Inclusion Body → organize into (EBs) → cell lysis & release of infectious (EBs)

(See diagram)



Summary of Clinical Syndromes Caused by *C. trachomatis* (genital) Sequelae

Local Infection		Complication	
Men	Conjunctivitis	<ul style="list-style-type: none"> • Prostatitis • Epididymitis • Reiter's syndrome 	Infertility
	Urethritis		
	Proctitis		
Women	Conjunctivitis	<ul style="list-style-type: none"> • Pelvic Inflammatory Disease • Perihepatitis • CIN • Reiter's syndrome • pregnant → Abort. 	Infertility Ectopic pregnancy Chronic pelvic pain
	Urethritis		
	Cervicitis		
	Proctitis		
Infants	Conjunctivitis	Chronic lung disease ?	
	Pneumonia		
	Pharyngitis Rhinitis / OM		

Male Infections

نحوه، علاج

A. Urethritis (NGU)

Male
Urethritis
(Ingeneral)

Male
GU NGU

urethral Inflammation can be Infectious or
Post Traumatic

Causes

Gonococcal Urethritis (GU)
(less common)

Non gonococcal Urethritis (NGU)
(More common sp. less promiscuous
High Socio Economi
Heterosexuals)

Known Etiology
(75%)

Unknown Etiology
(25%)

Non Specific
Urethritis
(NSU)

A. Common Causes:

- C. Trachomatis (D-K) (30-50%)
- Ureaplasma Urealyticum (20-40%)
- Mycoplasma Hominis (5-10%)
- Trichomonas vaginalis (<5%)

B. less Common causes:

- HSV
- LGV lymphogranuloma venereum
- Staph. saprophyticus
- Staph. viridans
- CMV
- Adenovirus

- UTI
- Urogenital TB
- SJS
- Acute Hydr. Cystitis
- Traumatic:
 - FB
 - instrumentation
 - Stricture
 - Stones
 - Oxaluria & Phosphaturia

Sexually transmitted urethritis

CIP of non gonococcal urethritis

- Asymptomatic → Soli.
- Symptomatic cases may be presented with:

Sexual
Instrumental

Sex
(Hx of)

IP: 2 ds - 4 ws

(just 2-3 wks)

Discharge: ch BY:-

Imp. test

- Thick
- Scanty

• Mucoid, purulent or Mucopurulent

• color
 green, yellow, Brown or Blood Tinged.

• Dysuria: ch BY:

meat. [inflammation]

- localized to meatus or distal penis
- Worst during First morning void (ad)
- ↑ Alcohol

• urgency & Frequency: Typically absent & if present will suggest Cystitis

• Itching: Sense of Itching or pruritus that Persist bet. voids. affect the urethra

• Orchalgia: Heaviness in the Genitalia & ass. pain in Testicles → suggest Epididymitis or orchitis.

• Complications: → Epididymo-orchitis, prostatic Reiter's.

• Sequelae: → Infertility.

• NB: there is Tendency For recurrence & chronicity.

Difference bet GU & N GU: (NG ch BY)

IP > GU
Disch.
 Scanty
 Thick
 Purul. or Muc. Pur.
 Cause: →

NB Types of urethritis

- ① GU
- ② NGU (subtye NSU)

③ Post gonococcal urethritis:

Type of urethritis ch. by

Start as GU + NGU (Chlamydial inf. usually ass. Gonorrhoea)



patient receive effective # for Gonorrhoea & not for Chlamydia



So after long period (IP in chlamydia is longer) after treating GU →

PGU.

So

Any case of GU → Treat Gonorrhoea & Follow this # by Antichlamydial Cause.

④ Recurrent or Persistent NGU:

def NGU that $\left\{ \begin{array}{l} \text{has } \geq 4 \text{ attack / year} \\ \text{or doesn't respond completely to \#} \end{array} \right.$ (after full #)

incid: 10% NGU.

Aetiology ① Insufficient antibiotic #.

② Resistant Antibiotic: Tetracycline - resistant *U. urealyticum*.

③ Reinfection ^{re-infection} (partner) or *T. vaginalis*.

④ Latent chlamydial inf.

⑤ organism protected in (sites) as prostate

⑥ Excess alcohol / Psychological: anxiety & frequent recurrent NGU.

⑦ UTI

⑧ Urethralgia

NGU ^{may be} obsessive exam. & squeezing urethra to prove

Women Inf. by chlamydia

♀ Genital Inf. Includes:

Cervicitis

- usually Asymptomatic (70-80%).
- when symptomatic → Non specific Symptoms as low back pain.

Specific signs (5-10%)

may include:

- ↑ mucopurulent endocervical discharge.
- ↑ Easy Cervical Bleeding

Urethritis

- usually asympt.
- Similar to ♂ urethritis
- Manifs. Worsened during Menses.
- May cause dysuria - pyuria Synd. - mimicking "Cystitis".

Complications:

① PID

- Chr. pain ✓ "iceberg!"
- Infertility ✓
- Ectopic pregnancy.

- may be Asympt.
- Milder Than That of Gonococcal inf.

③ Pregnant → Abort

④ CIN

⑤ Reiter's

② perihepatitis: (Fitz Hugh Curtis Synd).

Disorders Seen Both in ♂ & ♀

① Conjunctivitis (Inclusion Conjunctivitis)

• subinjection.

• follicular

Non purulent
(seropurulent)

↑ E.E.
Gonococcal
↓
purulent

② Proctitis:

• d.t. (Non) LGV. Sexually.

• AET ♂ : Homosexuality

• CIP ♀ : Anal sex or Complicating endocervitis.

Gonorrhea GI

③. Reiter's dis. = Reactive Arthritis (RA)
(Veneral Arthritis = Sexually Acquired RA)

- ① Urethritis (or \leftarrow Cervicitis)
 ② Arthritis
 ③ Conjunctivitis
 ④ Keratoderma, Bleorrhagicum. & Circinate
 Balanitis
 Vulvitis

def : Episode of Arthropathy occurring within 1 month
of an episode of urethritis, Cervicitis or Colitis

• • AET
(Unknown)

- ① Genetic → HLA B27

- ② Infective:

Post Venereal \rightarrow $\begin{matrix} (1-4 \text{ w}) \\ \text{NGU} > \text{GU} \\ \text{Mycoplasma} \end{matrix}$ (C. Trachomatis)

• post dysenteric → Shigella & Salmonella.

Others → *Strept. viridans*, *Mycoplasma pneumoniae*.

CIP

usually following
Inf. of
3.

- ① urethritis } C. Trachomatis > Gon.
② Cervicitis }
③ Colitis e.g. Shigella & Salmonella.

3
Main
Manifest.

- ①. Articular
- ②. Ocular
- ③. Muscat.

3
Rare
Manifest

- ① CNS
- ② CVS
- ③ systemic

- meningitis
- Encephalitis
- death ??
- Carditis
- Aortitis
- Arteritis
- Amphibolosis
- Generalized
- L.N
- Thrombo-phlebitis
- Amphibolosis

Arthritis:

d.t C. Trachomatis
Reactive
(Immunological)

But

d.t Gonorrhea is
d.t disseminate
from urethra to
Joint

① Articular → Poly-arthritis (Ch-G)

• Non suppurative.

• e in 1 m of Urethritis or Cervicitis or Colitis.

• Commonest joint →

Sacroileitis

Pain at back
& buttock;
↑ by rest.

• Other joints:

• Knee → Pain, Tenderness & Effusion.

• Small finger joints → Fusiform dactylitis,
Tenosynovitis,
Sausage digits.

② Ocular → usually Conjunctivitis.

③ Mucocut.

بثورات سطحية

Circinate Balanitis &
Vulvitis

Oral
ulcers

Keratoderma blenorrhagica
(Warty)

psoriasisiform & scaly
erythematous lesions

That begin as Vesicles
on Erythematous base

Progress To Macules, papules &
Nodules

"Painless" Erosive dermatitis e Small
ulcers on glans & vulva.

Invs

① D & Specific bact. inf. < Chlamydia Shigella, ...

② Arthralgias: to Exclude bact. Arthritis.

③ Acute Cases

• Neutrophilia
• ↑ CRP
• ↑ CS & CL
• ↑ ESR

④ Chr. Cases:

Normochromic ~
Normoglyc Anemia

Site / PP.
Scrotum & Nail
Scalp
Trunk

Treatment

Oral Cs
→ No Effect

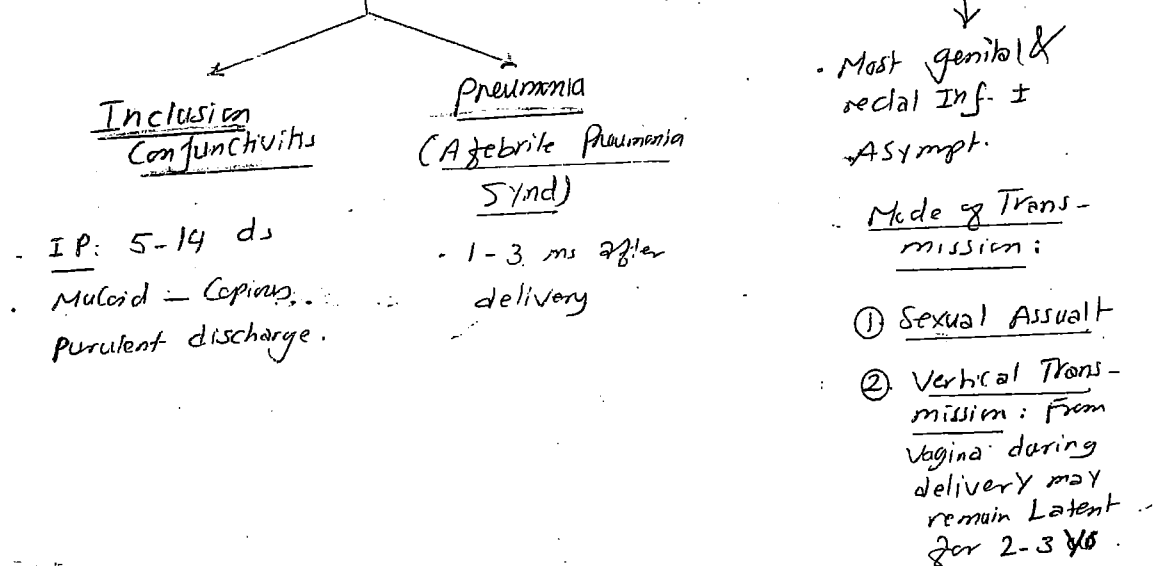
& Cervicitis.

① Urethritis & Colitis → Antibiotics

② Arthritis: NSAIDs (Indo- methacin)

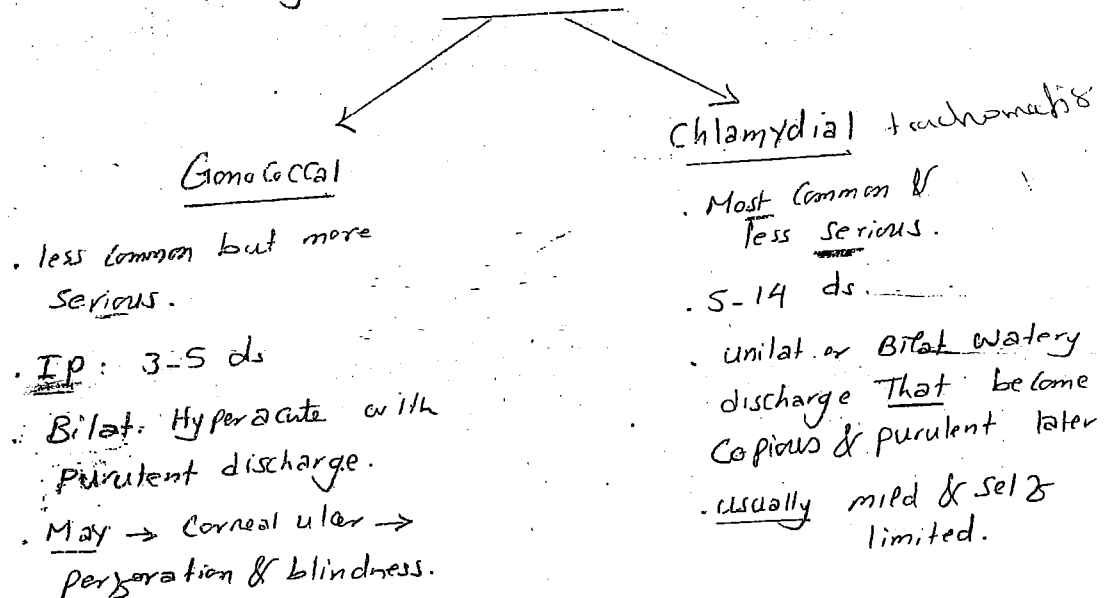
③ MTX & Azathioprine

Infants & Children Inf.



Neonatal Conjunctivitis (Ophthalmia Neonatorum)

- WHO def. Any conjunctivitis & discharge occurring during The first 28 days of life.



NB. other causes $\begin{cases} \text{Chemical (Silver Nitrate)} \\ \text{Viral (HSV)} \end{cases}$

Diagnosis of Urethritis

Alpisi 2 steps

- ① ID of Urethritis
- ② ID of AET

دفعه 1 → Urethritis can be diagnosed based on one or more of the following:

- ① Purulent or Mucopurulent urethral discharge.
- ② Urethral $\left\{ \begin{array}{l} \text{Swab or} \\ \text{Exudate} \end{array} \right\} \geq 5 \text{ WBCs / oil immersion Field}$
- ③ First voided urine that show:
 - WBCs esterase on dipstick test
 - or $\geq 10 \text{ WBCs / HPF}$

دفعه 2 → Then: All patients with urethritis should be investigated for NG & C. Trachomatis

Invs for Gonorrhea → NG
Invs for C. Trachomatis:

- ① Culture Techniques
- ② Antibody detection $\left\{ \begin{array}{l} \text{IgG} \\ \text{IgM} \end{array} \right\}$
- ③ Antigen detection $\left\{ \begin{array}{l} \text{ELISA} \\ \text{DFAT} \end{array} \right\}$
- ④ Gene detection $\left\{ \begin{array}{l} \text{DNA probe test} \\ \text{NAATs} \end{array} \right\}$

Specimen

في 2.5 و 10
Swab
Urine
Discharge

Can be obtained for
• Gram stain
• Culture
• IF
• Enzyme assay
• NAATs

NB • Urine specimen: Not used for Diagnosis of urethritis Except:

★ Dysuria + No Discharge → ① To Exclude Cystitis or Pyelonephritis
 is necessary if there is Dysuria without discharge.

?? $\begin{cases} \text{Cystitis} \\ \text{PN} \end{cases}$
 ↓
 (Urine analysis)

② if used for NAATs. → medic acid amplification test

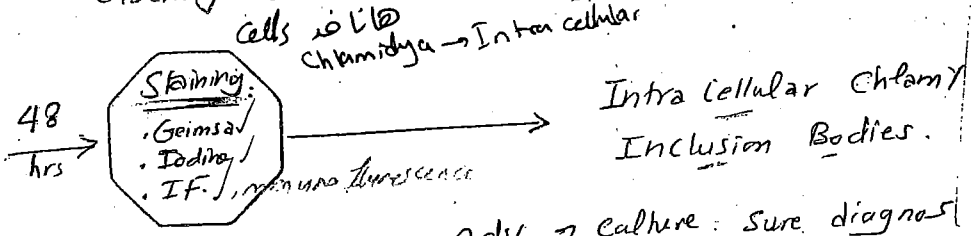
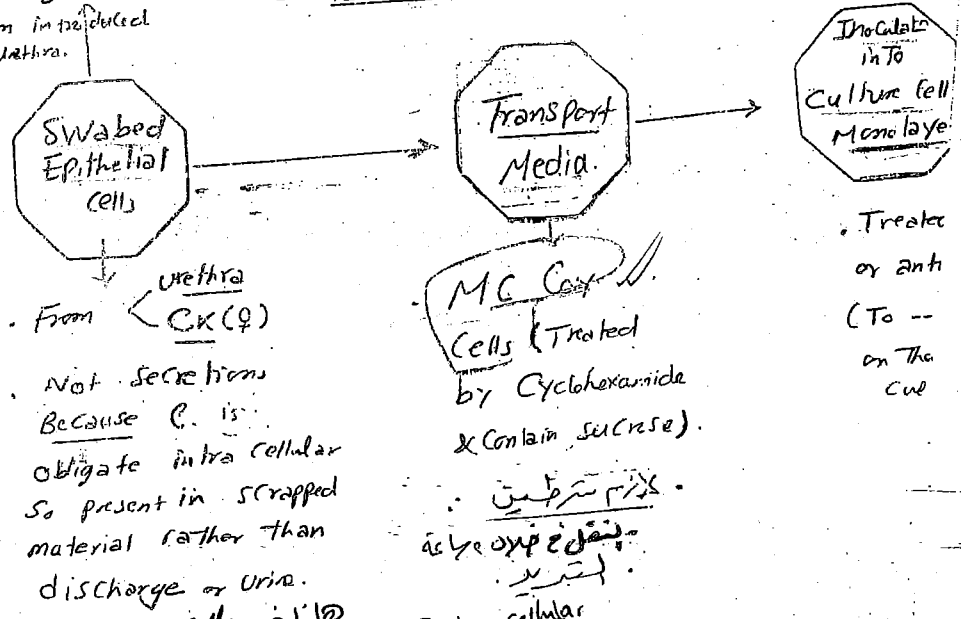
③ if " " D & T. vaginalis

Also Patients $\begin{cases} \text{GU: may have WBCs in urine} \\ \text{NGU: } \geq 30\% \text{ No WBCs in urine} \end{cases}$

Swab طريقة

- ① Cut alginate on non wooden stick
- ② 2 hrs after urinate
- ③ 2 cm introduced in urethra.

A Culture Techniques



Adv. of culture: Sure diagnosis
 may be used $\begin{cases} \text{pre HT to detect sensitivity} \\ \text{post HT to } \text{ " } \text{ Cure.} \end{cases}$

disadv. of Culture:

- ① High cost
- ② Not available in all labs.

not yet standardized
time consuming

② Antibody detection (Serology):

→ complement fixation test

done By $\left\{ \begin{array}{l} \text{CFT or} \\ \text{MicroIF.} \end{array} \right.$ to detect Antichlamydial Antibodies.

Adv & disadv.: of little significance due to high prevalence of IgG against chlamydia among the population.

But if $\left\{ \begin{array}{l} \text{IgM Abs.} \\ \text{4 times ↑↑} \\ \text{in IgG} \end{array} \right.$

→ Diagnose:
① Complicated cases, as Chl. Epididymitis, Salpingitis & Perihepatitis.

③ Antigen detection (Protein detect):

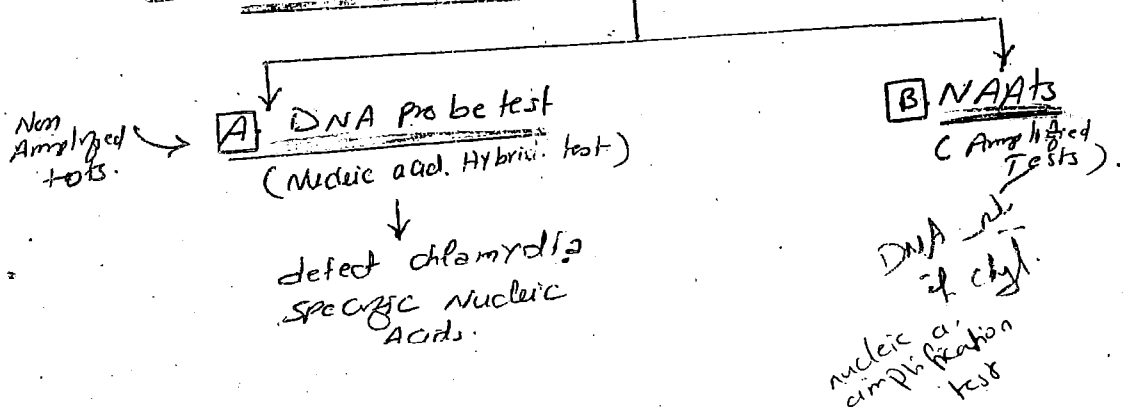
done By $\left\{ \begin{array}{l} \text{ELISA (Chlamydia Zima Test)} \\ \text{DFAT (MicroTrack test)} \end{array} \right.$

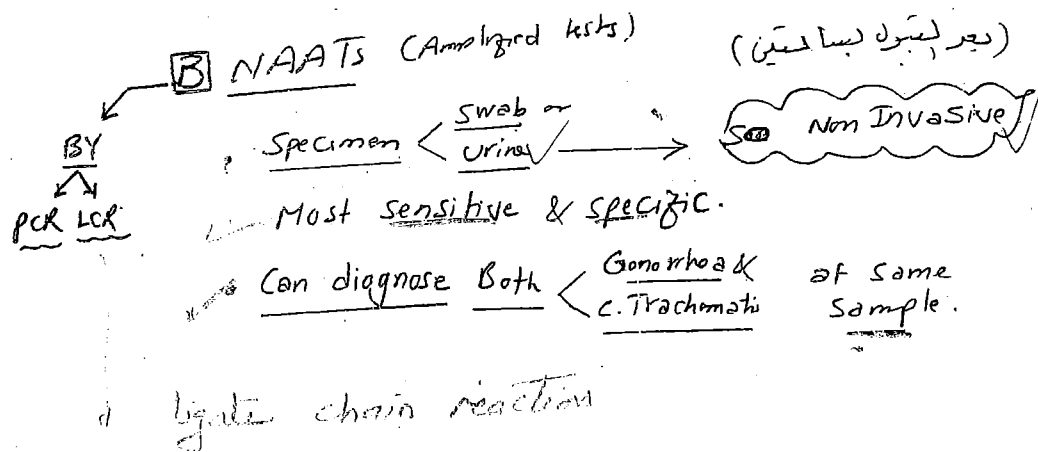
→ Direct fluorescent Ag test

- ✓ Sensitive
 - ✓ Specific
 - ✓ Cheap
 - ✓ Easy
- good correlation with culture.
→ can be done on dead organisms.

② N.C. Pneumoniae

④ Gene detection: By either





NB

Why #1 is difficult compared to Gonorrhea??

- ① Compliance : Antibiotic in \leftarrow GU \rightarrow Single dose
NGU \rightarrow Multiple doses.
- ② Cure Rate : In \leftarrow Gonorrhea : 95%
Chlamydia : 80%
- ③ Culture : In contrast to gonococcal culture; chlamydial cultures are
 - ① Expensive
 - ② Time consuming
 - ③ Not Always available

scull and
Ab del
Ay del
with 5
standard
cur rate 77

Lymphogranuloma Venereum (LGV)

(Etiomene, LG Inguinale, Nicolaï Favre dis)

• deg STD affect mainly the lymphatic system & caused by C. Trachomatis Serovars (L₁, L₂ & L₃).

Mode of Transmission:

(1) Sexual $\left\{ \begin{array}{l} \text{vaginal sex} \\ \text{anal sex} \\ \text{oral sex} \end{array} \right.$

(2) Non Sexual: (less common):

- Fomites
- nonsexual contact
- Lab. accidents (inoculation)
- Inhalation (creation of aerosols of the organism).

Sex: in ♂ 6 times > ♀. (but complications in ♀ > ♂ d.t. painless hidden nature of dis.)

Endemicity: Endemic in $\left\{ \begin{array}{l} \text{Africa} \\ \text{India} \\ \text{South America} \end{array} \right.$ (3rd stage)

Pathogenesis:

The organism enter the body via microscopic defects in genital Mucosa & skin → enter lymphatics → lymphangitis → lymphadenitis → perilymphadenitis & affection of multiple neighboring L.N.s → abscess formation → rupture → fistulae & strictures.

• In Rectum → destruction & ulcerate.

• Systemic affection: may occur.

CIP of L.R

Primary stage → 1ry or Initial manifs (Cutaneous Invasion) ^{بجريت}
(only in 25% of patients).

IP: 3-12 days.

There may be:

1. Primary lesion "Painless" ^{or} papule, Herpetiform vesicle, pustule, or ulcer

Ch ^{small} Transient Lymphangitis & dis. e Genital swellings

Site [♂]: Coronal Sulcus, Glans, Intramural p discharge.
[♀]: Vagina or CX, Vulva (Post coital)
^{♀ & Homosex}: Rectum.

2. Non Specific ^{urethritis} Cervicitis proctitis

Secondary Stage → Inguinal Synd (Lymphatic Invasion) ^{بجريت}
(♂ & ♀)

occurs after 10-30 ds - 6 mo. (2 wks after disappearance of 1ry stage)

Include 3: ^{Tender}
1. Bubo: unilat (70%), Enlarged Painful, Matted Inguinal L.N. (Fused Multiple Abscesses)

2. Groove sign: (Chic): The Inguinal L.Ns form 2 groups above & below ing. ligam [⊙] forms groove bet. them.

NB

1. Inguinal Synd.

is unusual in females as the draining L.Ns of Vaginal & Cervix are deeply seated in pelvis.

2. Constitutional Manifs Common e.g.

FAHN, EM, EN

3. Systemic spread of

C.T → pneumonia & Hepatitis.

③ Watering Pot or

Proctadenitis: L-Ns become matted →
Fluctuate → break through the
Inflamed skin → chr. discharging
sinuses.

Tertiary Stage

Genito-
Ano-rectal
Synd
(♀ > ♂)

(Lymphatic obst)

occurs after: ms - ys.

Sex

♀ > ♂ d.t spread from
vagina to rectum (or) d.
Anal sex.
♂ → Homosexuality

Include:

① Elephantiasis

Genitalia < Penis
L-Ls < Vulvae.

② Proctocolitis
(Granulomatous)

Scarring
Stricture
fistula of < Thigh
buttocks
urethra.

③ end stage

Ethiomena (Vulval elephantiasis &
Fistulae)
Saxophene (Penile Elephantiasis &
Fistulae)

④

فالج →

Cancer

See

Cause of
Death

proctitis →
perforation →
Peritonitis &
Cancer

Other manif

FAHM
Arthralgia
Meningitis & Encephalitis, Pneumonia.
Skin Rash.

inverted Frei
test

↑

INVS

① Frei test
complex

Intradermal test (discontinued in 1971)
Ag (Lygranum) containing Killed Agent → papule > 0.5cm

② CFT

sensitive (titer ≥ 1:16)

③ MIF

More " & specific (titer ≥ 1:512)

④ NAATS

PCR, LCR & (recently) Multiplexed Real Time
PCR.

⑤ Histopathology

⑥ Bubo Aspirate
& Culture (cell culture): 30% of Cases

Most
Specific &
Sensitive.

Micro immu

W.C.L.I
E.L.I.S

بفرس
(L1, L2, L3)
من سنجش

Treatment (2006 CDC STD Treatment Guidelines)

→ A. Treatment of uncomplicated genital chlamydial infections:

1. Recommended regimens:

Azithromycin, 1.0 gram orally in a single dose, or
Doxycycline 100 mg orally twice daily for 7 days (Some strains resistant).

2. Alternative regimens:

Erythromycin base 500 mg orally four times a day for 7 days, or
Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days,

or

Ofloxacin 400 mg orally twice a day for 7 days, or
Levofloxacin 500 mg orally once a day for 7 days.

→ B. Treatment of chlamydial infection in pregnant women:

1. Recommended regimens:

Azithromycin 1.0 gram orally in a single dose, or
Amoxicillin 500 mg orally three times a day for 7 days.

2. Alternative regimens:

Erythromycin base 500 mg orally four times a day for 7 days, or
Erythromycin base 250 mg orally four times a day for 14 days, or
Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days, or
Erythromycin ethylsuccinate 400 mg orally four times a day for 14 days, or

NB. Erythromycin estolate is contraindicated during pregnancy because of drug-related hepatotoxicity.

→ C. Treatment of neonatal conjunctivitis and/or pneumonia:

1. *Erythromycin base or ethylsuccinate 50 mg/kg/day orally divided into four doses daily for 14 days.*

2. Prophylactic antibiotic treatment for infants born to mothers who have an untreated chlamydial infection is not indicated. Infants should be monitored to ensure appropriate treatment if infection develops.

→ D. Treatment of chlamydial infection in children:

1. Children who weigh < 45 kg:

Erythromycin base or ethylsuccinate 50 mg/day orally divided into four doses daily for 14 days.

2. Children who weigh > 45 kg, but are < 8 years of age:

Azithromycin 1.0 gram orally in a single dose.

3. Children ≥ 8 years of age:

Azithromycin 1.0 gram orally in a single dose, or
Doxycycline 100 mg orally twice a day for 7 days.

→ E. Treatment of lymphogranuloma venereum: (ثلاث أسابيع)

1. Recommended regimen:

Doxycycline 100 mg orally twice a day for 21 days.

2. Alternative regimen:

Erythromycin base 500 mg orally 4 times a day for 21 days.

2 LGV 2011
م. ب. ق. د. هـ

NB. Some experts believe azithromycin 1.0 gram orally once weekly for three weeks is likely to be effective, although clinical data are lacking.

NB

No clinically significant emergence of drug resistance among CT strains. G. Patients should be instructed to abstain from sexual intercourse until partners are cured and for seven days after a single dose of azithromycin or until completion of a seven-day treatment regimen.

**Repeat testing after treatment for a chlamydial infection.*

1. Pregnant women: repeat testing, preferably by culture, 3 weeks after completion of therapy.
2. Consider test of cure 3 weeks after completion of therapy any time erythromycin is used.
3. All women with chlamydial infection should be encouraged to return for repeat screening approximately 3 months after treatment. Some experts also recommend men with chlamydial infection undergo repeat screening at approximately 3 months post-therapy.

The following antibiotics not used

1. Penicillin: very large dose needed/day (30 million/d).
2. Rifampicin: effective in vitro but resistant strains develop.
3. Aminoglycosides and cephalosporins (not effective).

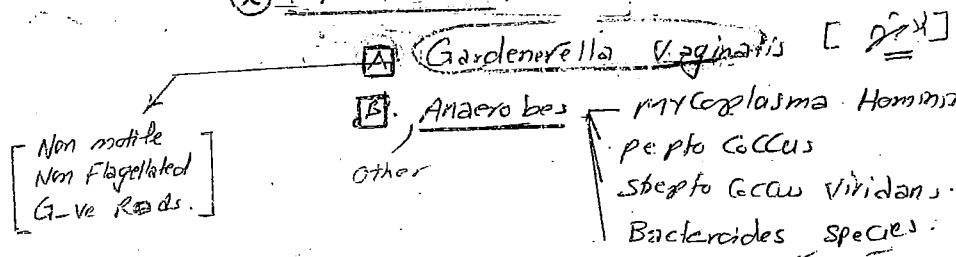
Bacterial Vaginosis (Non Specific Vaginitis)

Def Polymorphic Synergistic Inf. that may affect:

- ① Women → Colonization &/or Inf. of Vagina
- ② Men → Colonization of urethra (in men whose sexual partners have BV)

Aet: This Polymorphic Synergistic Inf. is due to 2 factors:

- ① ↓ Lactobacilli (NL Vaginal Flora) (± d.t.)
Antibiotics change pH
- ② ↑ Anaerobes:



Pathophysiology

NLLY: Lactobacilli are present in Large No in the vagina → liberation of H_2O_2 → Acidic pH (4-5) in vagina → growth of Anaerobes.

In BV: There is ↓ in No of Lactobacilli → ↑ pH → ↑ Gardnerella & other anaerobes.

Epidemiology

Age & Sex: all ages & sexes

Boys & girls → Colonization

Women → Colonization &/or Inf. of vagina

Men → Colonization not Infect. Affect

urethra of 80% of MEN whose wives (sexual partners) having BV.

Jejunum, Ileum, Cecum, ICD

D Mode of Transmission:

Sexually Transmitted

(STD لا ينتقل بالهواء)
GeLP

CLP =

Amsel's
Criteria
For
D.

(3 Needed For D)

① Discharge ch by:

✓ Smooth, Homogenous & grayish-white.

✓ Fishy Smelling (90%).

✓ Specially Noticed after sexual intercourse.

✓ Lack of Vaginal Inflamm.

• there may be ^{itching} irritatⁿ

(mis D as candidiasis)

(So better say
Vaginitis not
Vaginitis).

② PH ≥ 4.5 (NLY < 4.2)

③ +ve amine test: drop of vaginal disch. + drop of KOH (10%)

→ Fishy amoniacal odour (d.t
release of volatile amines.)

Whiff test

④ Clue Cell demonstration: (Pathognomonic)

drop of vaginal discharge

+

Saline drop.

↓
Clue Cells

(bacteria attached to vaginal epithelial cells)

* Culture of G. vaginalis: → (on) Blood agar medium → ① beta hemolysis on human Not horse blood

② Catalase & Oxidase -ve.

Asymptomatic

Complications:

① Sexual dysfunction (d.t bad smell).

② postpartum → Endometritis
Bacteremia
Neonatal infection

③ PROM & preterm labor (So Ht in pregnant women is essential)

Treatment:

① Metronidazole → 400mg twice 1 day x 5d.
2gm single dose

② if pregnant → Ampicillin 500 x 4 x 7.

③ Clindamycin Cream 2% IntraVaginally

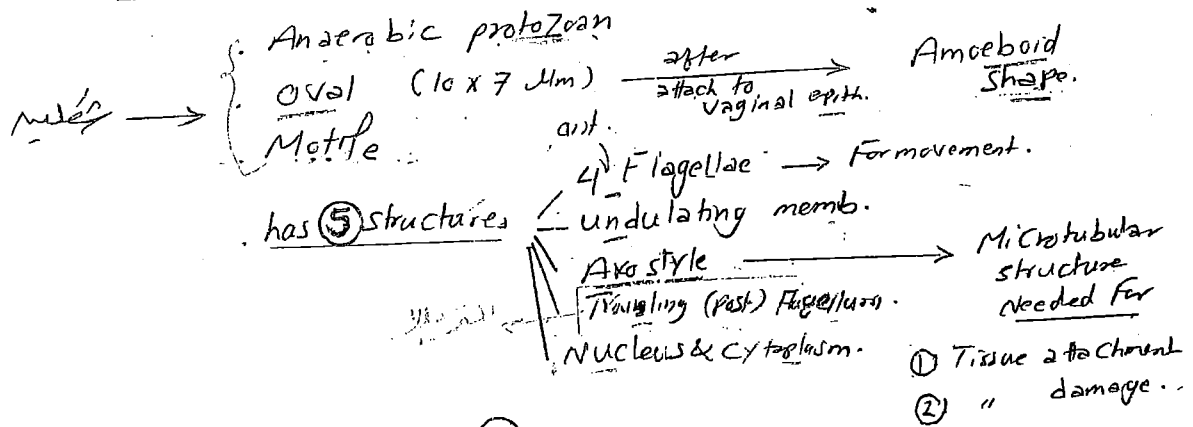
routine Ht of sexual partner Not recommended because Recurrence in ♀ not affected by Ht of the

معنى
بأنه لا يضر الزوج
في نقل العدوى

Trichomoniasis

Sexually Transmitted Infection Caused by

Trichomonas Vaginalis: usually affect ♀ (in ♂ usually Asympt)



Behavior ⑤

Chic jerky movement

Gonorrhea cells → infect sq. Epithelium e.g. Vagina

→ Can phagocytose other organisms (e.g. gonorrhea) inside cytoplasmic vacuoles

Needs Carbohydrate for their Energy & the Lactate is present in Vagina.

Can live for upto 24 hrs in moist environment.

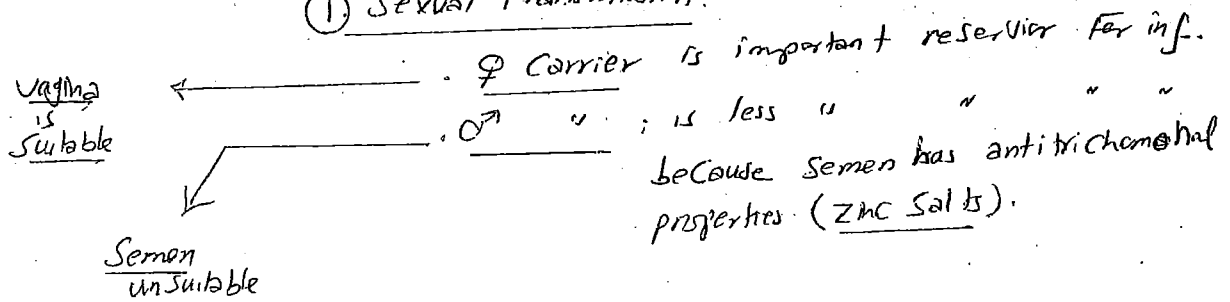
CHO Movem.
Inf
phago-
cytosis.

Live for 24 hrs in —

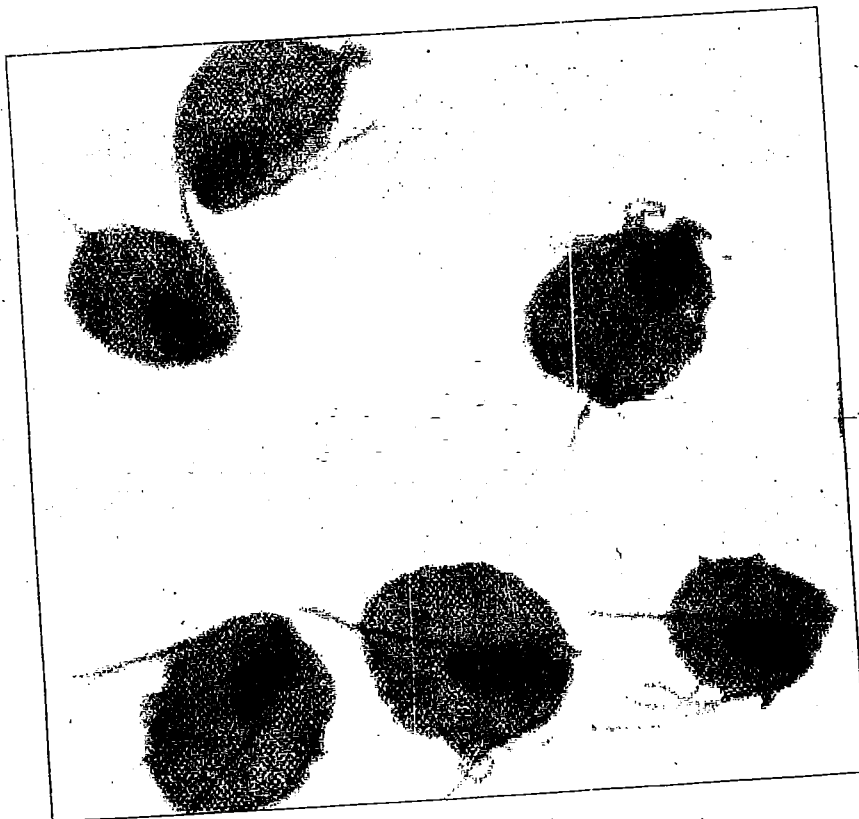
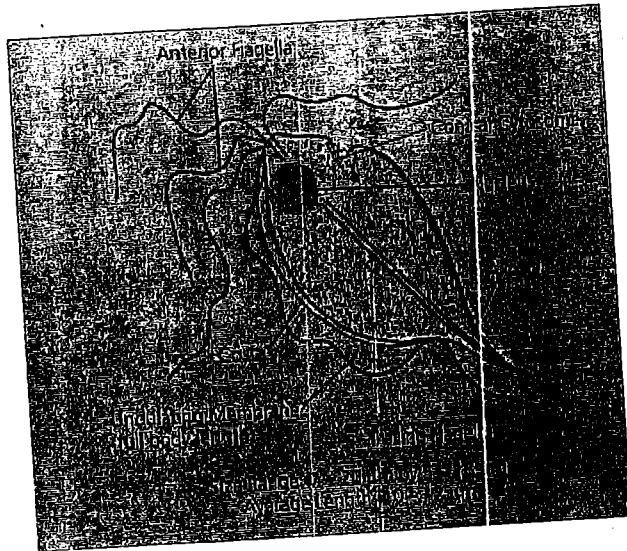
Mode of Transmission:

① Sexual Transmission:

From ♀ to ♂



TRICHOMONAS VAGINALIS



② Non sexual Transmission (... غير جنسي)

- ✓ Fomites
- ✓ Lavatory Seats
- ✓ Body Fluids {
 - Urine
 - Semen
 - Vaginal Exudate.

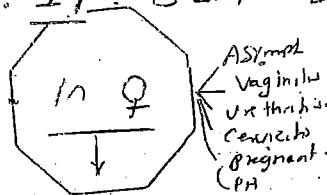
✓ Intrapartum → uncommon → Neonatal Trichomonal Vaginitis.
Through birth Canal.

Incid. T. Vaginitis commonly ass. with other Sexually Transmitted diseases:

- Gonorrhoea → 30%
- U. urealyticum → 95%
- M. Hominis → 90%
- Gardnerella V. → 90%

CIP

IP: 3 days - 3 w.



① Asymptomatic

② Vaginitis:

- Discharge {
 - profuse
 - yellow
 - irritant
 - Frothy
- Inflamed {
 - offensive.

↑ Menses & pregnancy

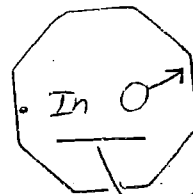
③ Urethritis (50%) → Dysuria, ...

④ Cervicitis: inflamed (strawberry ex)

⑤ ↑ PH: 5-8.

⑥ In pregnant {

- Preterm
- PROM



① usually Asymptomatic

② NGU (5%)

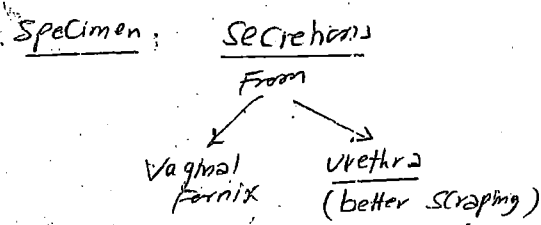
③ ulcerative balanoposthitis

- discharge:
 - Scabs, thick mucus or
 - Multipurulent & tickling in Urethra
 - Cholesterol after coitus.
 - Dyspareunia

Diagnosis

① Direct Mic Exam « Wet-Mounted preparation »
(wet smear)

Most reliable Method



discharge + saline
↓
Jerkly Movement

+ Saline drop

Dark Field illumination or Transmitted light

منظار

↓
Chic Jerky Movement of Flagellate.

- ② stained smear e Papanicolaou → less reliable.
- ③ Culture → Fineberg - Whittington for 4 hrs.
- ④ Exclude Other STDs.

Treat whole wife has Trichomonas to ↓ relif. & further spread.

Treatment

① Metronidazole: 2 gm single dose.

② For pregnant — after 1st trimester → Flagyl

Exclude ANY STD

Clotrimazole Vaginal pessaries

③ For Infants > 4m: Flagyl 5 mg/kg/day (For 3 ds).

④ Failed Metronidazole — Betadine Vaginal tab.

Metronidazole vaginal pessaries

Genital Candidiasis

(dimorphic Fungus)
↓

Candida: Yeast like organism present in 2 forms:

non pathogenic (Yeast) Form: present in

- GIT
- Vagina (20%)
- Rectum
- Mucocut. Areas
- Moist intertriginous areas
- Urine

Pathogenic (Mycelial) Form: → Causing Candidiasis.

Types

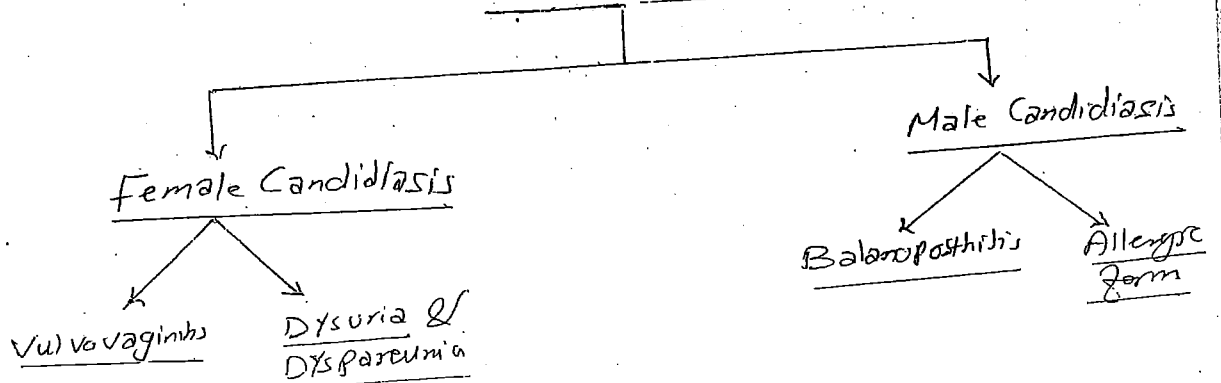
- Albicans (Commonest 80%)
- Tropicalis
- Pseudotropicalis (20%)
- Glabrata
- Krusei

Predisposing Factors:

• The conversion from non pathogenic (Yeast) to pathogenic (Mycelial) Form may occur under certain predisposing factors as:

- DM
- Pregnancy
- CS
- AIDS
- Antibiotics
- OCps
- Immunosuppressives
- Tamoxifen

CIP (may be asymptomatic)



Female Candidiasis

Vulva vaginal
(VVC)

Incidence & effect:

- (i). 75% of ♀s had an attack during their life.
- (ii) 30% → 8 pregnant.
- (iii) 15% → non "

CIP

Vulva → Tender, Painful, Edematous, Erythematous Eroded.

Vagina: → discharge:

- Scanty
- Thick
- Whitish (Crude-cheese like)
- Cheesy plaques on its walls → if removed → red hemorrhagic areas.

2P [PH: → NL (≤ 4.5). (mainly > 4.5)
[perimenstrual irritation may occur.

Patients w VVC can be divided into 2 main groups:

- ① Single or Few episodes → predisposing Factors can be detected
- ② Frequent Episodes (≥ 4 Symptomatic & Mycological proven attacks / year)

Dysuria & Dyspareunia

Vulval & Vaginal Irritation →

- dysuria
- dyspareunia
- Severe pruritus.

Recurrence

VVC e

No. Known

Ppt. Factor:

→ early sign

8

HIV

Mechanism of Recurrent VVC:

C. is useful clinical marker.

- 1. AIDS ^{Blastospores}
2. Candida may penetrate deeply into the vaginal wall → protected from topical H₂O₂ when menarche occurs → shedding of Epithelium → reemerge as viable organism.
- ✓ 3. Candidal reservoir in rectum

NB:

- Sexual Transmission of Candida in women is of Minor importance.
- Candida is not STD but ♂ contact should be seen if:
 - Symptomatic ♂ inf.
 - Recurrent ♀ inf.

Investigations:

1. Direct KOH For $\left\{ \begin{array}{l} \text{vaginal disch.} \\ \text{skin scraping} \end{array} \right.$ $\xrightarrow[\text{skin}]{\text{Gram}}$ Gram + Ve
 - Blastospores (Y)
 - Pseudo True Hyphae (M)
2. Culture on:
 - ① Sabouraud's agar $\xrightarrow[37^\circ\text{C}]{1-3 \text{ d}}$ Creamy, Moist Colonies
 $\xrightarrow[\text{Exam}]{\text{MIC}}$ clusters of budding cells.
 - ② Morse Neat agar $\xrightarrow[37^\circ\text{C}]{1-4 \text{ d}}$ C. albicans show $\left\{ \begin{array}{l} \text{Rounded} \\ \text{refractile} \\ \text{chlamydo} \\ \text{spores} \end{array} \right.$
 (this media differentiate bet. Albicans & others)
 - ③ Serum tube test $\xrightarrow{23^\circ\text{m}}$ Filament.

Chromogenic agars:

- Albicans ID agar
 - Candida colonies → blue
 - Other yeasts → white or Creamy
- Chrome agar
 - Albicans → green
 - Tropicalis → Blue
 - Krusei → pink

3. Commercial yeast identification system:

as . API 20 C
Aux color

4. Serology:

- Agglutinating & precipitating Abs.
- depend on cell wall Ag Mannan (of little value).

Treatment of VVC

- # of Predisposing Factors
 - Vaginal pessaries
(Corner stone of tx despite New Systemic antifungal)
 - # of Recurrent & chr. VVC
(see below)
1. Avoid vaginal trauma:
(as K-Y gel)
 2. Better Vaginal Hygiene:
(تجنب الإفراط في تنظيف المهبل)
(تجنب الإفراط في استخدام الصابون)
(تجنب الإفراط في استخدام المراهم)
 3. ↓ Candidal reservoirs in rectum:
Nystatin oral drops
 4. Control DM, Stop ^{stop} Antib. _{Tamoxif.}
1. Imidazole group:
 - Clotrimazole
 - Econazole
 - Miconazole
 - A. Clotrimazole
100 mg 1 night x 7 d.
or. 500 mg single night dose
 - B. Econazole
150 mg 1 night x 5 d.
 - C. Miconazole: (1200) mg
single dose.
 2. Nystatin
100,000 U
Intra-Vaginal
at bedt
for 3 d

Recurrent & chr. VVC:

(A) Remove predisposing factors e.g. OCPs, Antib.

(B) Systemic antifungals:

• Ketoconazole: 400 X 1 X 5 d (preferred)

• Fluconazole: 150 mg single dose

• Itraconazole: 600 mg single dose.

(C) longer course & vaginal pessaries

(Vaginal) (D) Boric acid 600 mg / d X 14 d

(E) # of ♂ partner.

NB

(1) Treatment of ♂ partner by either
Systemic or Topical Creams is essential

(2) Pregnant → Treatment by Vaginal
pessaries (Systemic is C.I.).

(3) Resistant cases usually d.t. *C. glabrata* &
Not d.t. *C. Albicans* is
resistant to Systemic Azoles (but)
responsive to Boric acid.

Male Genital Candidiasis

2 Forms

Candidal Balanoposthitis

- affect uncircumcised
- intense irritatⁿ of glans & prepuce = Erosion & white purulent discharge.

Allergic Form

Allergic reactⁿ of the or partner from infected woman

ch. by:

- itching
- Burning
- Small vesicles & Erosion.

ag^y → occurs shortly after intercourse

dramatic response

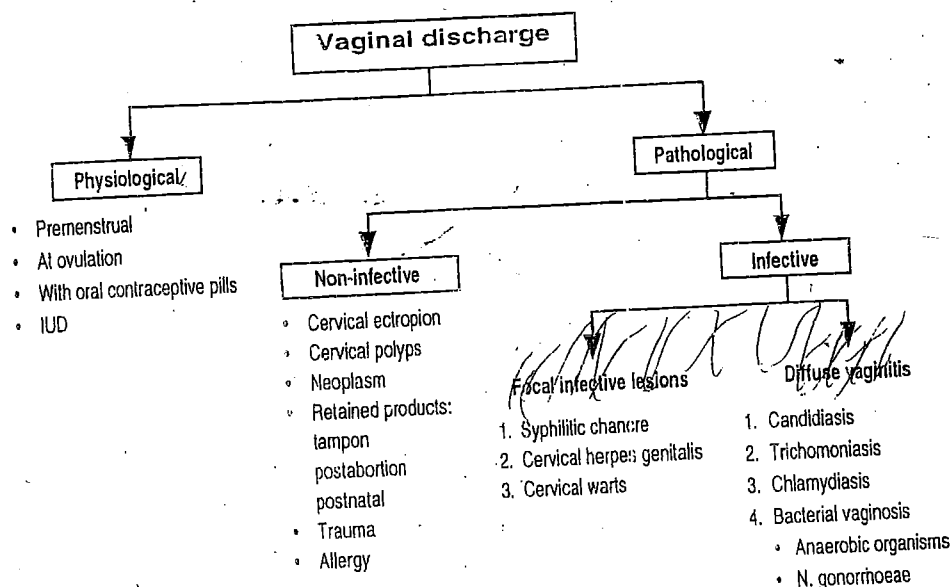
to

Hydrocortisone 1%

is

chic.

Vaginal infections ¹¹



I. History

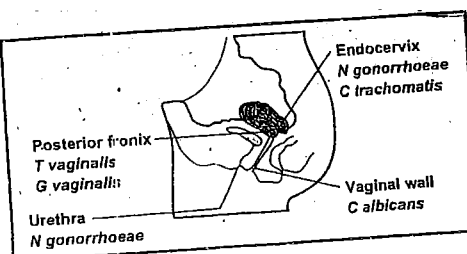
Certain points in the history suggest that STD is a possibility:

- A recent change of sexual partner.
- Recent multiple sexual contacts.
- Recurrent or persistent symptoms.
- Symptoms in her sexual partner, e.g.
 - Urethral discharge.
 - Irritation and redness of her partner's penis after sexual contact → *C. albicans*.
- General symptoms, e.g. abdominal pain, menstrual problems, rash, dyspareunia, arthralgia.

II. Physical and laboratory investigations

- The **physical signs** and **macroscopic appearance** of a vaginal discharge do not help in making an accurate diagnosis.
- Infection can be diagnosed accurately only after **microbiological tests** have been carried out on samples from the appropriate **anatomical sites**:

- Vaginal wall → *C. albicans*
- Endocervix → *N. gonorrhoeae*
C. trachomatis
- Urethra → *N. gonorrhoeae*
- Post. fornix → *T. vaginalis*
G. vaginalis



GENITAL ULCERS

سوال احتساب
XP

سوال ممکن ہے

- ① Genital ulcers
- ② Sexually or non sexually Transmitted genital ulcers.
- ③ single or Multiple genital ulcers
- ④ Painful or painless genital ulcer

سوال
XP

سوال ممکن ہے

1. Classification

Sexually or non sexually Transmitted
Single or Multiple,
Painful or Painless

2. Lab

1. 1st Classification

Genital ulcers

Sexually Transmitted

⑦

① 8 → 3 Types of ulcers

chance
Shall track
Gumma

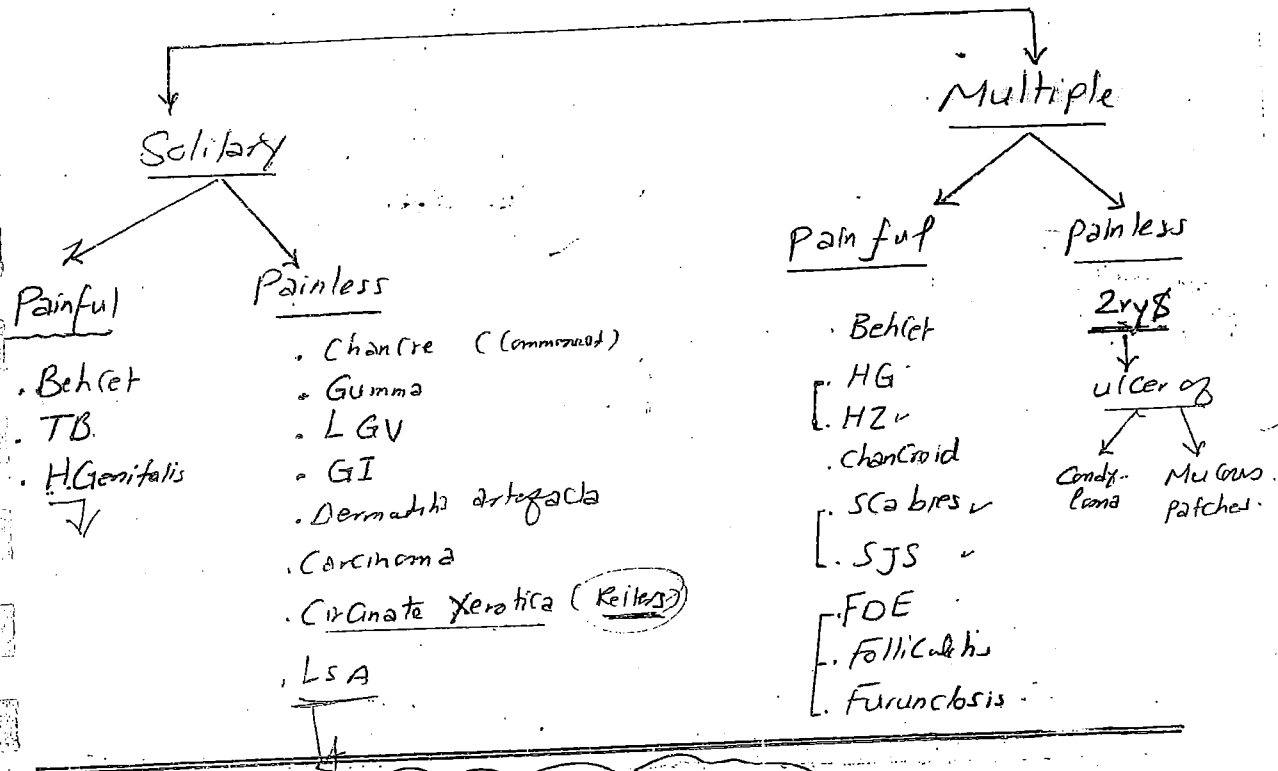
- ② chancroid
- ③ Granuloma Inguinale
- ④ LGV
- ⑤ scabies
- ⑥ HSV
- ⑦ HIV
- ⑧ other: Gonorrhoea, Trichomonas, Candida.

Non Sexually Transmitted

- ① Traumatic
- ② Tuberculosis
- ③
- ④ Behcet
- ⑤ HZ
- ⑥ My
- ⑦ FDE. (See Balunisi)

2. 2nd Classification

Genital ulcers



Reactive Genital Ulcers

نوع جديدي
 Culiets Vulvae Acutum = Lipschutz ulcer

Def: Non sexual, Non infective reactive genital ^{± oral} ulcerat^{ions} that follow an acute systemic illness.

Etiopathogenesis ?? • Exuberant Immune response to the original systemic Inf. ^{via} EBV
 • if recurrent it may be Complex Aphthosis or Behcet dis.

Cip Acute illness ← Tonsillitis, URTI, diarrhoea of Adolescent girls →

Painful vulvar ± oral ulcers ^{no} result → rarely occur.

Inv.: For EBV + Exclude other causes of Genital ulcers.

20) EXPY

Dez

AET

CIP

Inv.

HT

- [*happily!*
screaming]

- ① Traumatic: \leftarrow Soft superficial Tender d.t. lack of vaginal lubricant.

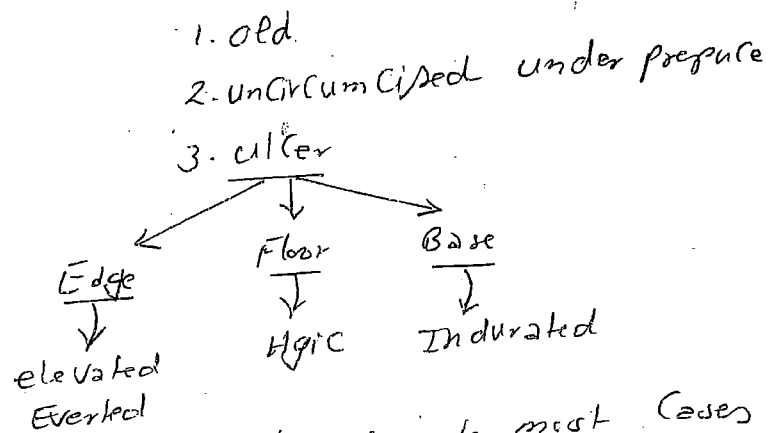
- ② Tuberculous $\left\{ \begin{array}{l} \text{undermined Edge} \\ \text{pale Granular} \\ \text{Floor} \end{array} \right. \rightarrow \text{Post. scrotal (d.t} \\ \text{extension from} \\ \text{TB Epididymitis)}$

- ③ β → Ovae passed into urine & Faeces → Some deposited in the skin → Angenital ulcer & Nodules.

4. Behcet $\therefore \rightarrow$ Recurrent $\left\{ \begin{array}{l} \text{Genital ulcers} \\ \text{oral ulcers} \end{array} \right.$ [البثور من Behcet]
+ ocular Manifests + others

5. H-Z \rightarrow Multiple grouped vesicles on
Erythematous base \rightarrow ulcer [البثور الحادة]
Vulva penis

6. Mg ulcers \rightarrow Bowen's & SCC of penis



4. Phimosis : In most cases \rightarrow Obscure the ulcer

5. 2nd bact. Inf. (90%)

6. Enlarged Inguinal L.N

either due $\left\{ \begin{array}{l} \text{Cancer} \\ \text{Inf.} \end{array} \right.$ or

Diagnosis of Genital ulcers

Diagnostic clues

① Traumatic → نَجْدٌ بِمِخْرَعةٍ
بَعْدَ جُلْدٍ

② Behcet → oral genital

③ Herpetic → نَجْدٌ

④ H. Z → Dermatoma

⑤ Mg → عِلَق

Nodule plaque ulcer
Single at scrotum or penis

Biopsy for SCC.

⑥ FDE: Recurrent at same time after intake of same drug.

Lab

عِلَق

No genital ulcer diagnosed without Lab. Invs.

① DG → For serology Biopsy
chance ulcer → Not for Gumma
mildness forbes

② Chancroid: Stained smear from G.T of ulcer → Giemsa Wrights
also culture
Klebsiella granulomatis appe: as clusters of blue organisms with chic "Safety Pin"

③ LGv: Culture from the ulcer → C. Trachomatis.

④ HSV2 → Tzanck culture IF

⑤ Mg: if suspected → Biopsy.

[DMN2 &
Emed.

Balanitis

- Def : Inflammation of glans penis
• More common in uncircumcised
• prepuce is usually involved

→ Balanoposthitis

Predisposing Factors:

1. DM.
2. Irritation by
 - Smegma
 - urine alkalies
 - Ext. contacts
3. Trauma
 - Clothing Friction
 - long foreskin
4. Pathogens
 - Yeasts
 - Vaginal
 - Chlamydia
 - Viruses

Caused

A. Infectious Causes

B. Non Infectious Causes

A. Infectious causes

① Fungal: (Candidal)

• Commonest cause

• there are 2 Forms < ... (See genital candidiasis)

② Bacterial: May be d.t

Genitococcal
? Chlamydia

• in associates w N GU

• similar to that of Reiter's

• Mycoplasma: in ass. \bar{e} Mycoplasma NGU.

Balanitis (rare)

- Following chancre
- glans: whitish coalescent plaques on edematous background.

✗ Fournier's Gangrene: (Necrotizing Fascitis of Genitalia)

• Cellulitis $\xrightarrow{\text{Progress to}}$ painful blue-brown Ecchym. discoloration

- Etiology: Bacteroids + G-ve bacilli
- pre-dis. factors: DM
- #: broad spectrum Antibiotics

Anaerobic Erosive Balanitis

Backenash
• G-ve bacilli
• Anaerobic
• Flora of GIT
• B. fragilis

- d.t: Bacteroid
- clp: Erosive gangrenous Balanitis
- #: Flagyl

Group B beta Hemolytic Streptococci

- Commonest cause of Bact. balanitis
- Erythema & Edema of glans & C. sulcus
Coronal

③ Para Sitic:

Amoebic Balanitis

d.t Entamoeba histolytica

④ Protozoal:

Trichomonas Balanitis

30% of Men \bar{e} Trichomonas Balanitis
or without

: Flagyl

Non Infectious Cause

① Circinate Erosive Balanitis: See Reiter's

② Balanitis Xerotica Obliterans:

عروة
خشنة

- LS 7 genitalia
- C.I.P. • Ivory-white, itchy, Maculae on glans
- Phimosis may occur (if prepuce affected)
- Malignant Transformation may occur.

③ Zoon Balanitis (plasma cell balanitis):

• affect old or middle Aged uncircumcised

• Etiology: unknown but may be d.t. react response to:

Considered as:

• persistent chr. idiopathic form of balanitis

infective
irritative
injury

بكتريا
التهاب
[ps] [IN] [ACD]
↓
A

C.I.P. • Single or Multiple glistening plaque(s): e:

- tiny erosion
- Most
- Minute red specks (Cayenne pepper's Sp)
- persists for many years

• pathology • Dense band like infiltrate of Plasma Cells [lichenoid]
• Capillary dilatation
• Hemosiderin deposits

• (H) Cs, Gentamycin, Cor laser, IL IFA-α.

4. Micaceous & Keratotic Pseudoepitheliomatous Balanitis

Balanitis:

Prep $\left\{ \begin{array}{l} \text{start as Coronal balanitis} \rightarrow \text{Silvery} \\ \text{white appearance of Mica like} \\ \text{Crust} \\ \downarrow \\ \text{Keratotic Horn Masses on} \\ \text{glans} \end{array} \right.$

with loss of prepuce Elasticity.

Path: Pseudoepitheliomatous (Hyperplasia in reaction to infection).

5. Other Causes

(A) FDE:

lesion $\left\{ \begin{array}{l} \text{Early: red oval or rounded swollen, } \pm \\ \text{blistering patches} \\ \text{Late: purple-brown color} \end{array} \right.$

Sites: Hand, Feet & genitalia.

Drug: may be: NSAIDs, Sulpha, Tetracycline

onset: 30 min - 8 hrs after intake.

(B) Dermatitis

(C) Psoriasis

(D) L-P

(E) PIN (Penile intraepithelial Neoplasia) \rightarrow Bowen's dis

(F) Scabies.

!!: Acc. to the cause

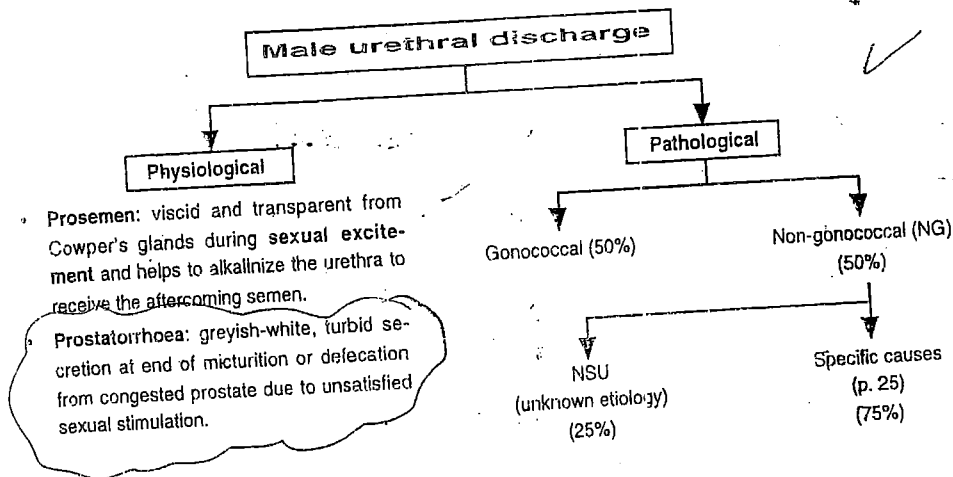
Complications of Balanitis:

(1) phimosis

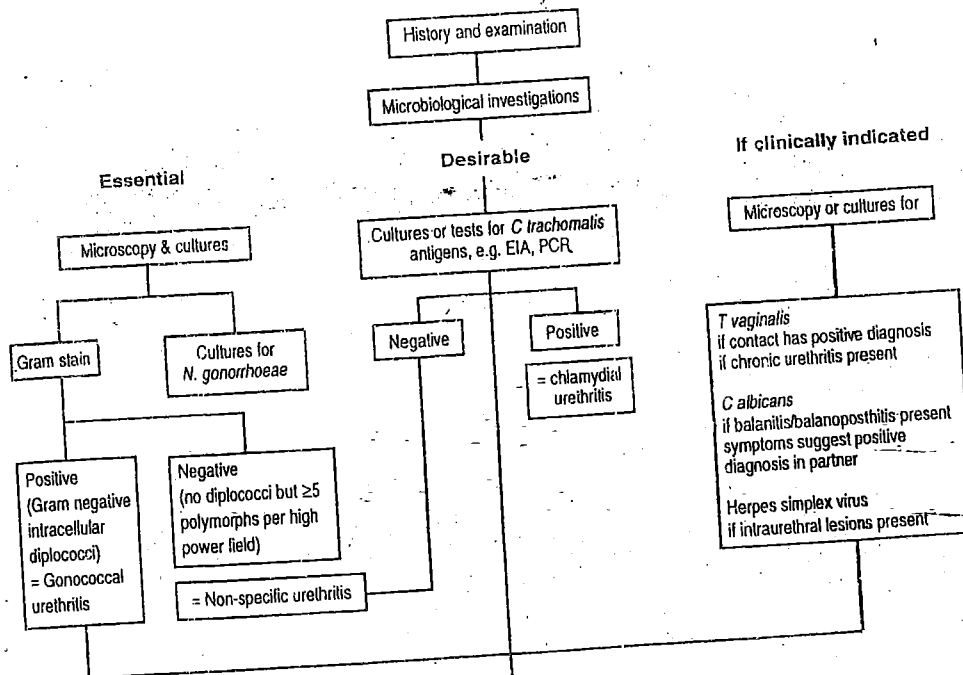
(2) MG

Male urethral discharge: Diagnosis

It is the commonest presenting symptom of STD in men.



Investigation of urethral discharge



Urine testing \leftarrow two glass test
protein, sugar

- Serological test for syphilis + offer HIV test - Hepatitis B serology in homosexual men
- Investigate sexual contacts

I) History

A) Of urethral discharge

1. Site:

- Urethral infection
- Subpreputial infection in uncircumcised men, e.g. herpetic or candidal.

2. Quantity and color of discharge:

- Profuse yellow or green → gonorrhoea.
- Scanty clear or white → NGU.

3. Duration (IP)

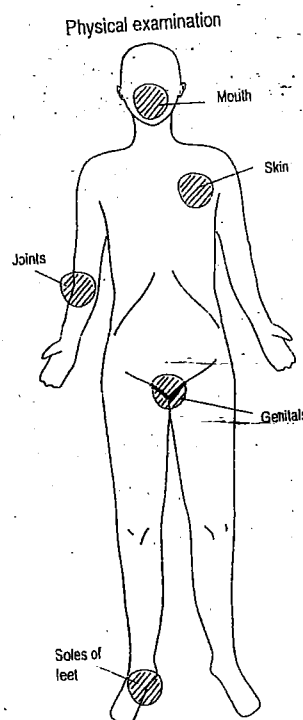
- Gonorrhoea: 2-5 days.
 - Chlamydia or other types of NGU: 7-14 days.
- NB: 5-10% of patients with G or NGU are asymptomatic.

B) Sexual history

1. Number and type of sexual contacts (homo- or heterosexual) in the previous 4 weeks.
2. Homosexual: which anatomical site(s) have been exposed to risk, e.g. rectum, throat, urethra or combination of all three.
3. Sexual contact in other countries: because of the development of resistant strains of N. gonorrhoea to penicillin in some countries.
4. Number of partners and tracing of sexual contacts: ? to determine the source of infection.

II) Examination

1. Genitalia, pubic hair and perianal area.
2. General examination: to exclude possible complications of G and NGU.
3. Examination of skin, soles of feet, mouth and joints.
4. A specimen of urethral discharge must be collected for Gram staining and microscopical examination for **Gram -ve intracellular diplococci**.
 - Present → Gonorrhoea
 - Absent + presence of ≥ 5 pus cells / HPF → NGU.
 - *C. trachomatis* cannot be identified by direct microscopy.
 - *T. vaginalis* (only in patients with chronic urethritis and in those whose female sexual contacts already have trichomoniasis). A specimen of discharge is placed on a slide (with one drop of saline), a coverslip added and examined without staining under microscope with dark ground illumination.



III) Culture

As up to 10% of cases of gonorrhoea may be missed if microscopy alone forms the basis of diagnosis, specimens of urethral discharge should be cultured for *N. gonorrhoea*.

IV) Confirmatory tests, serological tests and urine tests.

Management of urethritis "Urethral discharge"

- Men should be examined when they have not voided as long as 4 hours.
- Urethra should be stripped from posterior to anterior to detect urethral discharge if it is not present spontaneously.

I) Peripheral clinic without microscope

1. Clinical differentiation between gonorrhoea (= profuse, spontaneous yellow or green discharge) and NGU (= scanty discharge which must be expressed in order to be seen, clear or white as it contains fewer PMNLs). Patients fail to respond to penicillin for gonorrhoea may have penicillin-resistant gonorrhoea or NGU.

2. Effective treatment for both conditions:

- Tetracycline 500 mg orally 4 times daily for 7 days, or better
- Spectinomycin 2 g IM (single for gonorrhoea), followed by tetracycline 500 mg orally 4 times daily for 7 days for NGU.

II) Peripheral clinic with a microscope

- Confirm urethritis by presence of ≥ 5 pus cells in a stained smear of urethral contents. Examine smear for Gram -ve intracellular diplococci.
 - If Gram -ve intracellular diplococci are present → treatment of patient and sexual partner(s) for gonorrhoea.
 - If no such diplococci → treatment of patient and sexual partner(s) for NGU.
 - 1st choice: tetracycline 500 mg by mouth 4 times daily for 7 days.
 - 2nd choice: erythromycin (not estolate) 500 mg by mouth 4 times daily for 7 days, especially in pregnancy.

III) Intermediate Clinic

- Culture for *N. gonorrhoea*.

IV) Central laboratories

- Test for *B. lactamase*.
- Isolation and identification of *U. urealyticum*.
- Isolation, identification and serotyping of *C. trachomatis*.

Genital dermatoses

A. Itching

B. Pain

C. Infect

D. Lesions

A Genital Itching:

- . pruritus Ani
- . Balanitis
- . pruritus Vulvae
- . ECZema (AD, SD, CD, LSC & Intertrigo)
- . others: ps, LP & LS.

B Genital pain:

- . Balanitis
- . Dyspareunia & Vaginismus
- . Behcet-
- . LP
- . FDE
- . Crohn's
- . Pudendop ~~Neuro~~ ^{algia}
- . entrapement Synd.
- . Dyesthesia

others.

- . reactive genital ulcer
- . Plasma Cell Vulvitis
- . Atrophic - Vulvovaginitis
- . Desquamating Vaginitis

C. Infect of Genital skin (♂ & ♀)

Sexually Transmitted

- . ~~♂~~
- . Gonorrhoea
- . Chlamydia
- . LGV
- . Chancroid
- . G. Inguinale
- . Trichomoniasis
- . Candidiasis
- . others
 - . H. genitalis
 - . Genital Warts
 - . Molluscum

. pubic louse & Scabies

Non-Sexually Transmitted

- (1). Bact.: Boils, Impetigo, TB Erythrasma, BV
- (2). Viral: molluscum, Warts, HSV & HZ
- (3). Fungal: T. cruris & Candidiasis
- (4). Parasitic:
 - . Pubic lice & Scabies
 - . leishmaniasis
 - . Amebiasis
 - . Filariasis
 - . Shistosomiasis

D. Genital Lesions

• Hidradenoma

(H: H

S. PIN

• VIN

• SCC

• Leiomyoma

• EMPD

• PD

• Early penile papules

• Steatocystoma

• Nevi & melanoma

• Angiofibroma

• Milia, epid. cyst

• Calcinosi

Complications of common genital infections²

Complications		Infection		
		Gonococcal	Chlamydia Positive	Negative
Women				
• Local:	Pelvic inflammatory disease	+	+	+
	Bartholinitis / abscess	+	-	-
• Systemic:	Disseminated infection	+	-	-
Men				
• Local:	Epididymitis / orchitis	+	+	+
	Prostatitis (± vesiculitis)	+	+	+
• Systemic:	Reiter's disease	-	+	+
	Disseminated infection	+	-	-

Sexually transmitted arthritis

1. Disseminated gonococcal infection.
2. Reiter's syndrome.
3. Hepatitis B virus.
4. Lymphogranuloma venereum.
5. Syphilis of joints:
 - a) Secondary syphilis: painless arthritis, tenosynovitis, bursitis or generalized painful arthralgia.
 - b) Tertiary syphilis: arthralgia, synovitis or arthritis, bilateral bursitis of Verneuli, juxta-articular nodes.
 - c) Late congenital syphilis:
 - Bilateral hydroarthrosis (Clutton's joint).
 - Von Gies joint.
 - True arthritis.
 - d) Tabes dorsalis: Charcot's joint.
6. Others:

Mycoplasma hominis	Epstein Barr virus
Ureaplasma urealyticum	Cytomegalovirus
HSV	Chronic meningococemia

Anti

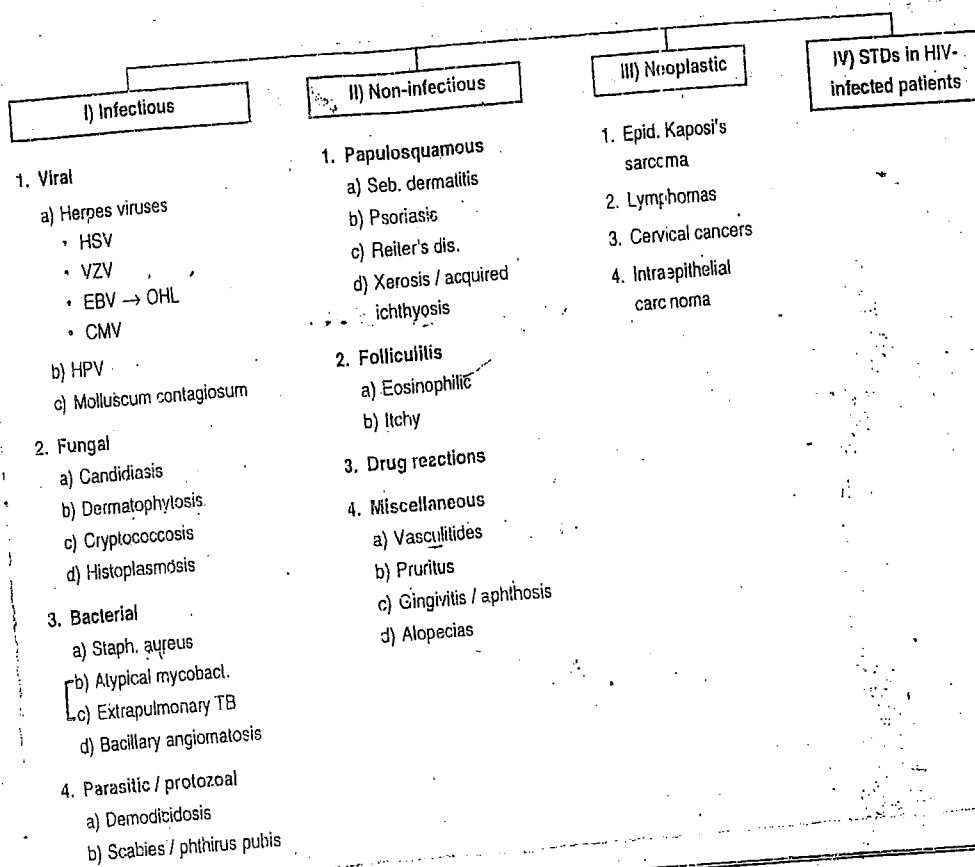
17. STDs

Chancroid

	Chancere	Soft Sore
1. IP	9-90 days	3-5 days
2. No. of lesions	Single	Multiple, may be kissing ulcers
3. Pain	Painless	Painful
4. Edge	Sloping	Ragged undermined
5. Base	Firm, indurated	Soft
6. Bleeding	Does not bleed easily	Bleeds easily
7. Ooze	Serum	Seropus
8. Lymph nodes	Painless, discrete, firm, never suppurate	Tender, matted, suppurate & form sinuses
9. DG	+ ve	- ve
10. Treatment	Penicillin	Azithromycin, ceftriaxone

Mucocutaneous manifestations of HIV disease

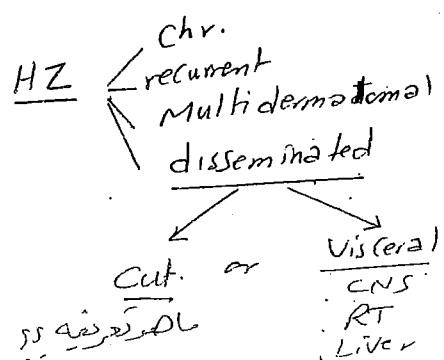
دالة
نحو



HSV inf. differs in HIV pts. than in healthy in that

- Clinically
- 1. large irregular chr. Erosion or ulceration
 - 2. disseminated lesions
 - 3. Severe digital inf.
 - 4. Herpetic proctitis.

Foscarnet may be needed while others may be ineffective why??



A large perineal ulceration(s) in a person with risk factors for HIV infection, should be considered HSV until proved otherwise.

3. EBV → Oral hairy leukoplakia (OHL)

- affect 50% of HIV pts after 5-10 yrs.
- also may affect any Immunosuppressed Patients.

• Site → Ventrolateral border of Tongue as
asymptomatic { grayish-white
 Corrugated
 don't rub off.

• Prognosis: OHL { 48% → will develop HIV
 in 16m.
 80% → after 30m.

• Trt → oral Acyclovir 400 x 5
 Foscarnet.

4. CMV → ^{common} Commonest virus Co-infect with HIV Patient → Dissemination to many organs + Cut. { ulcerative vesiculobullous lesion. vasculitis.

5. HPV

- ① ↑ Facial & Intra-oral Warts
- ② difficult to treat Condyloma Acuminata
- ③ CIN.

6. Molluscum { Wide spread Inf.
Giant Molluscum → Cidofovir.

Fungal Inf.

1. Candidiasis — Mucocat. is Very Common
It → Digestion.

It \rightarrow Digital can.

Trachea
Oesoph
pharynx

2. Dermatophytes → wide spread inf.
①. *T. pedis* → d

① *T. pedis* → diffuse hyperkeratotic

② OM (شعری: ای نزع)

(Proximal subungual) (PSO)

3. Disseminated $\begin{cases} \text{Histoplasmosis} \\ \text{Cryptococcosis} \\ \text{penicillinoses} \end{cases}$

Bact. Inf.

i. Staph → (Commonest).

1. $Sapn \rightarrow$
2. MAC (MAIC) & extra pulm. TB.

3. ~~8~~

3. \$
4. Bacillary Angiomatosis → (BA)

dog

Bact. Inf. caused by G-ve bacilli

Genus Bartonella:

1. B. henselae: \rightarrow Most cases of $\angle \frac{CSD}{BA}$ &
Some BA.

2. B. Quintana — Some BA.
Trench fever

3. B. bacilliformis → Bartonellosis (Includes Chr. cut. lesions of Verruga Peruana)

2501

• CIP 1. HX Contact with Infected Cat.

Transmission may be through Scratching & Flea

H. cut systemic

2. Papules & Nodules / single or Multiple (Hundreds)
red - violaceous vascular
simulating:-

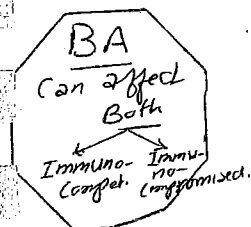
- PG
- Hemangioma
- Kaposi's Sarcoma.

3. Systemic spread → Liver, spleen & Lung →
Fever & wt loss.

• Histopathology → Stain: Warthin - starry Silver

- ① Epith. Cellarettes
- 5 ch ② lobular prolif. of small Bvs
lined by Large protuberant cells.
cuboidal
- ③ Edematous Stroma
- ④ Leukocytic infilt. & Lymphocytic debris.
- ⑤ Granular clumps of purplish material (clusters of bacteria)

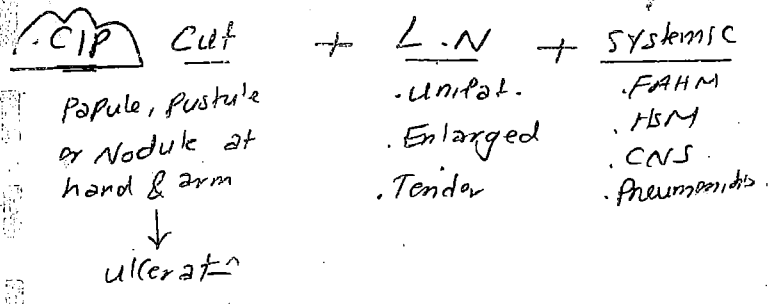
• Tx → 1. Erythromycin 500 x 4 /d.
2. Doxy.



BA Associated diseases +

CSD

- Bg. & self limiting
- 90% → History of CS
- Commonest Cause of Bg
- Chr., Adenopathy in Children & Adults



path → an tr in val

Bartonellosis (Carrión's dis)

AET B. Baciiformis.

CIP: 2 phases

Oroya Fever (Acute Endemic phase)

- In Non Immuned
- 100% of RBCs are Parasitized
- Hemolytic anemia
- Macrocytic Hypoch. an.
- RES infilt.
- L.N
- High MR d.t. anemia, septicemia, reactivate of TB.

Verruga Peruana

- In Partially Immuned
- 2ms after the Febrile stage.
- lesions
 - Maculopapular Erythem. in Extremities + Face.
 - Soft Hemangiomatous S.C Nodules.

#	1. PCN	4. Chloramphenicol
	2. Streptomycin	(PCN ← 1st / 2nd)
	3. Tetragline	

Parasitic & Protozoal Inf.

① Demodicosis:

Demodex folliculorum → itchy follicular, scaly
erythematous papules (pityriasis folliculorum)
Face
Head
Neck

Ht → Antiscabietic
Ivermectin
Permethrine
Crotamiton
Sulfur
Metrifluralone

② Scabies

either Classical or
Crusted

DD From ps & SD

by

Hyperkeratosis
Crusting
Fissuring
Nail dystrophy

Ht → Keratolytics + Antiscabietic

Non Infectious Manif.

[SD
Xerosis] [ps
Reiter
Folliculitis
DE]

"Skin"

Most common cut. manif.

① SD

ppp
ppp
ppp

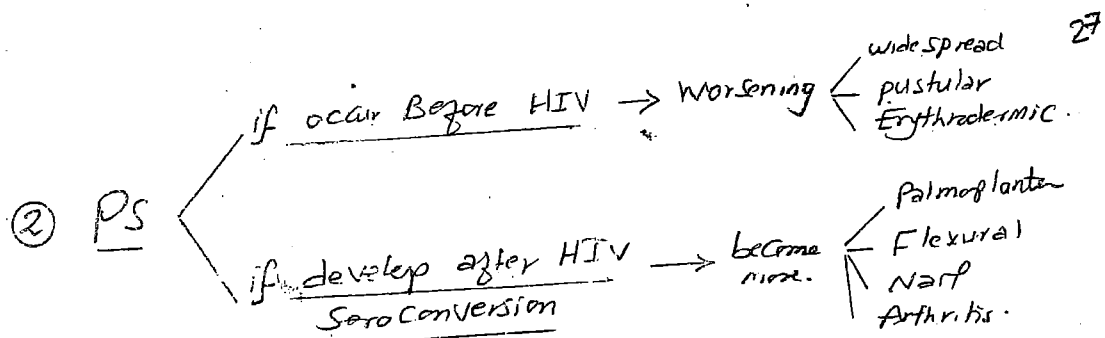
Frequently its The First diagnostic clue.

CIP → as usual SD.

Path. → differs From SD in NL Individual imm.

→ Dermatitis Interface React.

Ht → as usual SD



③ HH

- Topical HH: as usual
- phototherapy: Care is it as it may aggravate KS.
- Systemic HH:
 - MTX → leucopenia.
 - Cyclosporine & etretinate → good effect CD4 affected
 - Zidovudine → marked improvement.

③ Reiter's → more severe in HIV.

④ Xerosis → generalized pruritus.

d.t Malabs & diarrhea.

Folliculitis

Eosinophilic Folliculitis (EF)

occur in advanced cases (CD4 < 200)

Follicular urticarial Papules:

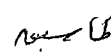
- Severely itchy
- Celestex into → plaques & papule vesicular border
- at: Head, neck, upper back & upper arms.

Pruritic Papular Eruption of HIV (Itchy Folliculitis) (PPE)

severely itchy
red or skin colored
papules on same
distribution of EF.

Criteria for D of EF.

A Clinical Criteria:

- follicular urticarial papules.
- severely itchy.
- distribution → 

B Histopathology: Eos ^{↑ Infil.} _{← Spongiosis Abscess}

- Folliculo centric inflamm (Mainly Eos. but others ±)
- follicular spongiosis.
- eosinophilic follicular Abscesses.

C Lab Criteria:

- +ve HIV serology
- -ve invs for _← ^{Bact.} _{Fungi}
- peripheral Eosinophilia.
- ↑ Ig E
- CD4 < 200.

NB → PPE & EF → may be the same dis.

Cut. Drug Eruptions: (dit _← ^{altered Metabolism} _{↑ basophil Reactivity})

- Common in HIV patients specially
- Sulphonamides (> 50% of cases).

Mycoplasma Infections

(125-250 nm)
 (deg) The smallest Free living microorganisms
 That lack the cell wall. So $\left\{ \begin{array}{l} \text{Not stained by Gram} \\ \text{NOT susceptible to} \\ \text{beta lactams} \end{array} \right.$

They usually resides (NL Inhabitants) eg The
 Mucosa of $\left\{ \begin{array}{l} \text{RT} \\ \text{GUT} \end{array} \right.$ but never penetrate it. Except

If there is $\left\{ \begin{array}{l} \text{Immunosuppression or} \\ \text{Instrumentation} \end{array} \right.$ \rightarrow Invade the blood \rightarrow

dissemination To Many Organs.

Need $\left\{ \begin{array}{l} \text{cholesterol} \\ \text{urea} \end{array} \right.$ for growth.

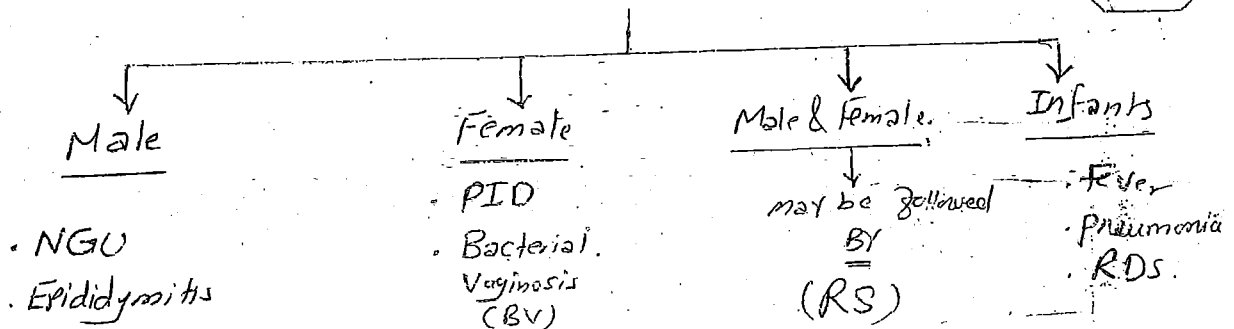
It has 3 Types:

- ① Urea plasma Species $\left\{ \begin{array}{l} \text{urea plasma urealyticum} \\ \text{urea plasma parvum} \end{array} \right.$
- ② M. Hominis
- ③ Other species $\left\{ \begin{array}{l} \text{M. Genitalium} \\ \text{M. Penetrans} \end{array} \right.$

Diseases Caused by Mycoplasma

$\left\{ \begin{array}{l} \text{Genital:} \\ \text{Cutaneous:} \end{array} \right.$

U. urealyticum
 Colonize:
 5-20% M
 40-80% F



NB Cut. diseases caused by it:

- SJS
- EN
- Gianotti-Crosti synd.
- urticaria
- Morbilliform rash
- Acrocyanosis.

- U. urealyticum \rightarrow NGU & pneumonia
- M. hominis \rightarrow post partum fever
- M. genitalium \rightarrow urethritis

Lab. Diagnosis

- ① Culture: Not indicated as routine Test but its main indication is (persistent) NGU that's -ve for Chlamydia In order To do antimicrobial sensitivity Test To direct the tt.

Media

• Mycoplasma Media
• Stuarts

Needs ★

• N₂
• 10% CO₂
• 37°C

Swab: Taken & streaked on "Mycoplasma/urea plasma selective" medium That

Contain:
• agar base
• yeast
• horse Serum
• Mg⁺⁺ Sulphate
• Urea / Ampicillin

Incubate Anaerobically
For 48 hrs at 37°C. 10% CO₂
N₂

Fried egg colonies

To differentiate
bet. the 2 →

U. Urely.
• small (5-10µm)
• brown color
• color change in media containing Urea

M. Hominis
• large (40-50µm)
• color change in media containing Arginine.

② ELISA & CFT:

Treatment ① Tetracycline: effective against Chlamydia & Mycoplasma

② Erythromycin: as in Chlamydia.

③ Azithromycin

④ others

• clindamycin

• Levofloxacin & ofloxacin.

NB

• U. Urealyticum

→ Erythromycin

• M. Hominis

→

Incomparable
effect to not
other species.

Chancroid

No Induration (Soft Sore - Soft chancre, Ulcus Molle)

def STDs caused by G-ve bacilli "H. ducreyi" &

- Ch. by:
- Acute genital ulceration
 - Inguinal adenitis (buboes)
 - NO systemic manifs.

Epidemiology:

Most painful ulcer

Incidence → The commonest cause of genital ulcer in many developing (poor) countries.

Age: ~30 Ys (age of Maximal sexual activity)

Sex: M:F = 10:1 (M: Uncircumcision, Heterosexuality, Promiscuous practice)

organism: → Haemophilus Ducreyi

G-ve bacilli (Facultative anaerobes)

Small size & typical chaining pattern

Transmission

Prostitutes

High
prevalence

Can survive only in high Turn over
of sex partners → so unsuitable
in areas with low rates of partner change
"multi"

Pathogenesis: organism inoculation occurs via microscopic
barrier defects in Epid. → Th-mediated
Inflamm. & → regional Adenitis.

CIP

IP : 3-7 days (or 8d - 3 w.)

Start as : papule → pustule → ulcer.



(can)

Kissing ulcer

No → usually multiple (may start single & d.t. apposition → multiplicity & ± coalesce → Giant ulcer)

Site : The commonest site in:

Male

Foreskin (prepuce) Ext or Int

Others sulcus
frenulum
Glans
shaft

Female

Labia Majora

other L. minora
Thigh
Cx
perineum

Size : 2mm - 2cm.

Shape : irregular or serpiginous.

Edge : undermined & ragged.

Floor :

Covered by GT
Purulent ✓
Exudate

Base : soft (not indurated).

Fixate : Not fixed.

Tenderness → +ve (Most painful genital lesion).

Discharge → Purulent. Urethral discharge
 In case of urethral lesions.

L.N. / +ve in 50% (M > F)
 usually unilat.

Tender, Fixed, matted → ulceration through skin

↓
 Skin Under-structures

↓
 discharging sinuses & fistulae.

→ Pathognomonic signs for Diagnosis:

- ① Genital ulcer ^{Multiple.} _{Sgt} Painful & Tender
- ② Inguinal L.N. ^{Tender} _{Suppurative} (bubo). ^{unilat.}

→ Criteria for Diagnosis:

- ① 2 Clinical - (Pathognomonic).
- ② 2 - ve Inv. _{dark ground mic. & Serology for} ^{Tests for} HSV.

Diagnosis:

- ① Stained smear: Swab from the ulcer will show ^{Extracellular} G-ve ⁺ Cocci bacilli in many patterns:

Chain pattern
 - Single clusters
 - Schools of fish
 - railroad tracks
 - Fingerprints
 → usually Extra-cellular PMNL Cyp

disadv / Non Sensitive / Specific (many other bacteria may be similar to it & many specimens don't show the organism)

② Culture:

The accepted standard for *D.* (60-80% Sensitivity).

Media: Nairobi Media consists of

Biplate of:

Campylobacter
agar base

+ 2% Hb

+ 5% Fetal

Calc Serum

Muller Hinton agar

+ 5% chocolateized horse blood.

③ PCR: replace The Culture in many centers.

good on samples prepared from *H. ducreyi* Culture.

less sensitive when used to Test genital ulcer specimen.

④ Multiplex PCR:

(Simultaneous
amplification of
DNA Targets
from *H. ducreyi*
& other organisms)

التهاب، ulcer, *H. ducreyi*, HSV
عينة من *H. ducreyi* & *HSV*

⑤ Monoclonal Antibody: detect *H. Ducreyi* on ulcer specimen.

⑥ Serology: Not useful.

⑦ Pathology → Not recommended for *D.* only For Excluding Malignancy in Non Healing lesions

⑧ Tests for *D.* & other STDs: & HIV

3 Zones:

- Peripheral: Neut. + fibrin + RBCs + Necrosis
- Mid: New Blood v. + endothelial Cell prolif. → occlusion → Thrombosis
- Central: dense plasma cells & Lymphoid Cells.

DD → Genital ulcer (8P. 7) داء

AZithromycin → 1gm single dose
Ceftriaxone → 250 mg single IM dose.
Ciprofloxacin → 500 mg x 2 x 3.
Erythromycin base → 500 mg x 4 x 7

also
sulfa

NB. The partner from 10 ds preceding the onset of symptoms should be examined & # offered.
Patients with chancroid + HIV → same # regimen but with more prolonged period.

NB: Chancroid & HIV:

Incid. of HIV Inf. & Transmission is markedly ↑ in presence of Genital ulceration

Genital lesions therefore become both: ① a portal of entry for non infected individuals ② Exit for already HIV infected persons.

2. In H. ducreyi ulcer: There is ↑↑ No. of Macrophages & CD4, both ↑↑ Expression of Chemokine receptors < CCR5 & CXCR4 These are 2 main Co-receptors essential for HIV entry.

RANTES Chemokine: ligand for CCR5 → present in papular & pustular stages of d.p.

NB. CCR5 & CXCR4: belong to class 7 Transmembrane G-protein coupled receptors.

علاج لقرحة داء تناسلي
طفاضة مع اريز

Granuloma Inguinale = Donovanosis

(Granuloma Venereum)

def: rare chr. progressive ulcerative bacterial infection (G-ve)
 caused by Calymmatobacterium (Klebsiella) granulomatis

Causative organism: Klebsiella granulomatis; G-ve bacilli.

Mode of Transmission $\left\{ \begin{array}{l} \text{STD} \\ \text{Vertical (via infected birth canal)} \\ \text{Fecal contamination} \end{array} \right.$

Pathogenesis:

The 1st lesion: Small cut $\left\{ \begin{array}{l} \text{Papule or} \\ \text{Nodule} \end{array} \right.$ contains
 Mononuclear cells & Cytoplasmic Vacuoles
 Filled with microorganisms which will rupture \rightarrow
 release of "Donovan bodies"

CIP (IP 9-90d).

Genital lesions:

Papule or nodule ch by:

Red Painless $\xrightarrow{\text{Eros}}$ Beefy
 granulomatous ulcer with rolled
 edges (Painless genital ulcer)

L.N: Not affected Except if:
 2nd bact. inf. or
 Extension of inflamm. to it.

If untreated: lesion may remain dormant or
 progress slowly involving whole of

Healing: \rightarrow severe fibrosis & tissue destruction.

Extragenital lesions:

\pm d.t. \uparrow either Auto inoculation or
 2nd to dissemination

Site:

Commonest \rightarrow Bone
 Others \rightarrow Skin, Intra-abdominal cavity &
 oral cavity.

Ulcer:
 Beefy
 Painless
 Granulomatous
 Edge: raised
 rolled

Ext. genital &
 Inguinal Area

Site of genital lesions

Male
 . prepuce
 . glans
 . frenulum
 . coronal sulcus

Female
Commonest
 is Vulva.

"V.A.G."
NO
LN (Except
 if 2ry bact.
 Inf.)

Clinical Varieties:

① Ulcerative (most common):

arise from the nodular type

ulcers are by (large)
 spreading
 painless
 Exuberant

② Becomes red & bleed easily

③ Edge → raised rolled

④ Base → clean friable.

② Nodular Type (see before): may be similar to Lymphoma (Pseudobubo)

③ Cicatricial Type: Dry ulcers evolve into cicatricial plaques & may be ass. with Lymphoedema.

④ Hypertrophic or Verrucous.

ulceration
 nodular
 1-2 mm

In later stages of the dis →

Elephantiasis

Diagnosis (Stained smear - Culture - PCR - Serology - Pathology &...)

① Stained smear: From Tissue scrapings stained

with $\begin{cases} \text{Giemsa} \\ \text{Wright} \\ \text{Leishman} \end{cases}$ Stain \rightarrow Donovan Bodies

Vacuoles containing bacilli in Macrophages or PMNL.

Morphology $\begin{cases} \text{Coccoid} \\ \text{Coccobacillary} \\ \text{Bacillary} \end{cases}$

Staining: \rightarrow Bipolar staining present at 2 ends of the organism \rightarrow

"Safety pin" appearance

② Culture: \rightarrow difficult; can be done

No Artificial media

on $\begin{cases} \text{Human peripheral blood Mononuclear Cells} \\ \text{Hep 2 cells} \end{cases}$

③ Histopathology:

(Also to Exclude Carcinoma)

(Biopsy & Tissue Crush Preparation):

\rightarrow safety pin appearance

Biopsy or scrap from ulcer

Edge

Crushed bet. 2 glass slides

Separated, air dried & stained

Safety pin appearance of

Donovan Bodies

④ PCR (under trial)

⑤ Serology \rightarrow Not useful.

Complications

- . Unilateral Strabismus & dermoids
- . Rectovesical Fistulae in M
- . Elephantiasis of genitalia & L.L
- . Superinf. by Fusiform bacilli → Phagedenic ulcer.
- . SCC.

Treatment

(علاج)

- ↓
1. TMP & SMX + Doxy 100 X 1 X 2
 2. Azithromycin
 3. Cipro 750 X 2/d + Erythromycin 500 X 4/d
 4. Norfloxacin.

ماجستير تناسليه (3)

S.T.D

د/هانی ابوالوفا

2017

د. د. د. د.

just print

01025329200- 0502200362

HIV disease (AIDS)

1st 2313616

def

HIV dis. disease ch by defective cell mediated immunity occurring in persons with no cause of immunodeficiency other than HIV.

White

AIDS: Severe end stage of HIV dis. ch by $\left\{ \begin{array}{l} \text{CD4} < 200 \\ \text{opportunistic Inf.} \\ \text{Mg.} \end{array} \right.$

History of Epidemics

Origin: From non Human primates in sub-saharan Africa & Transferred to humans by direct contact during Hunting or butchery.

(دکتر)
Subsaharan Africa
منطقه آفریقای جنوبی
منطقه غربی
منطقه شرقی
منطقه مرکزی

History of the epidemic	
1981	Cases of pneumocystis carinii pneumonia and Kaposi's sarcoma in the United States.
1983	Discovery of the virus.
1984	Development of antibody test.
1993	CDC definition of AIDS: all those with confirmed HIV infection + CD4 count $< 200/\text{mm}^3$ + indicator dis.

Luc Montagnier et al

2nd

Table 22.3: Nomenclature of AIDS virus

1983	Lymphadenopathy associated virus (LAV)
1984	Human T-lymphotropic virus type 3 (HTLV-3)
	AIDS related virus (ARV)
1986	Human immunodeficiency virus (HIV)
1987	HIV-1 and HIV-2

HIV
Virology

- Class
- Ch
- Structure
- replication cycle
- Types
- Epidemiology

Zalcitabine

1-5-11g

PN
gene
CLT ulce
Transmission

Class:

Genus: Lentivirus

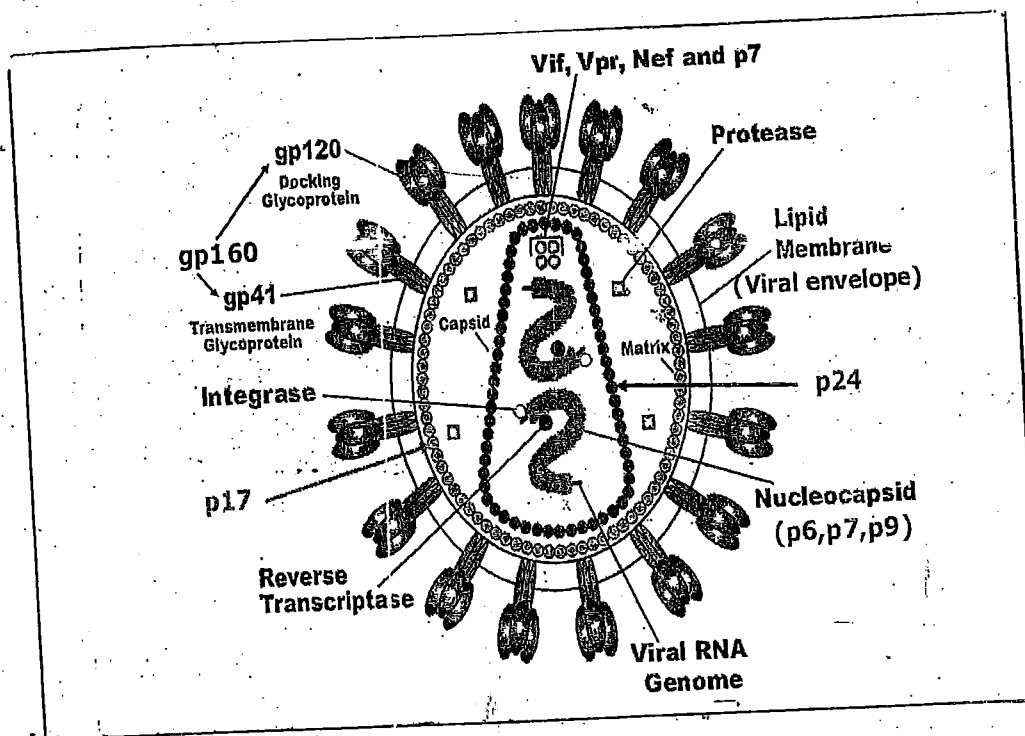
Family: Retrovirus (Retroviridae = Contain ENZ. Reverse Transcriptase)

General Characters:

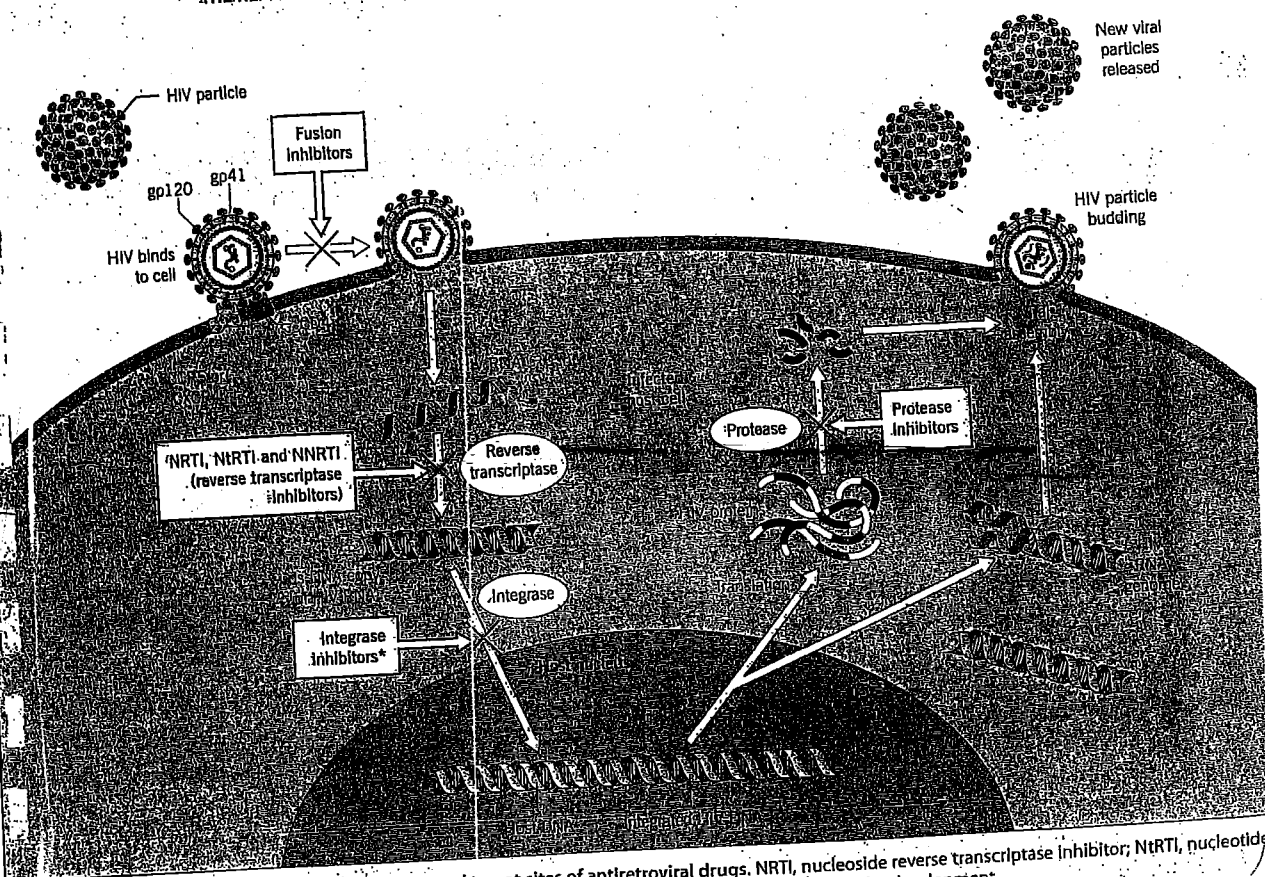
1 RNA virus (Contain 2 single RNA Strands)

2 Reverse Transcriptase ENZ. (Can make "Transcribe" DNA copies from its RNA inside the Host cells in a Repodirection)

الإنزيم الذي يحول RNA إلى DNA



THE REPLICATION OF HIV WITHIN CD4⁺ LYMPHOCYTE AND TARGET SITES OF ANTIRETROVIRAL DRUGS

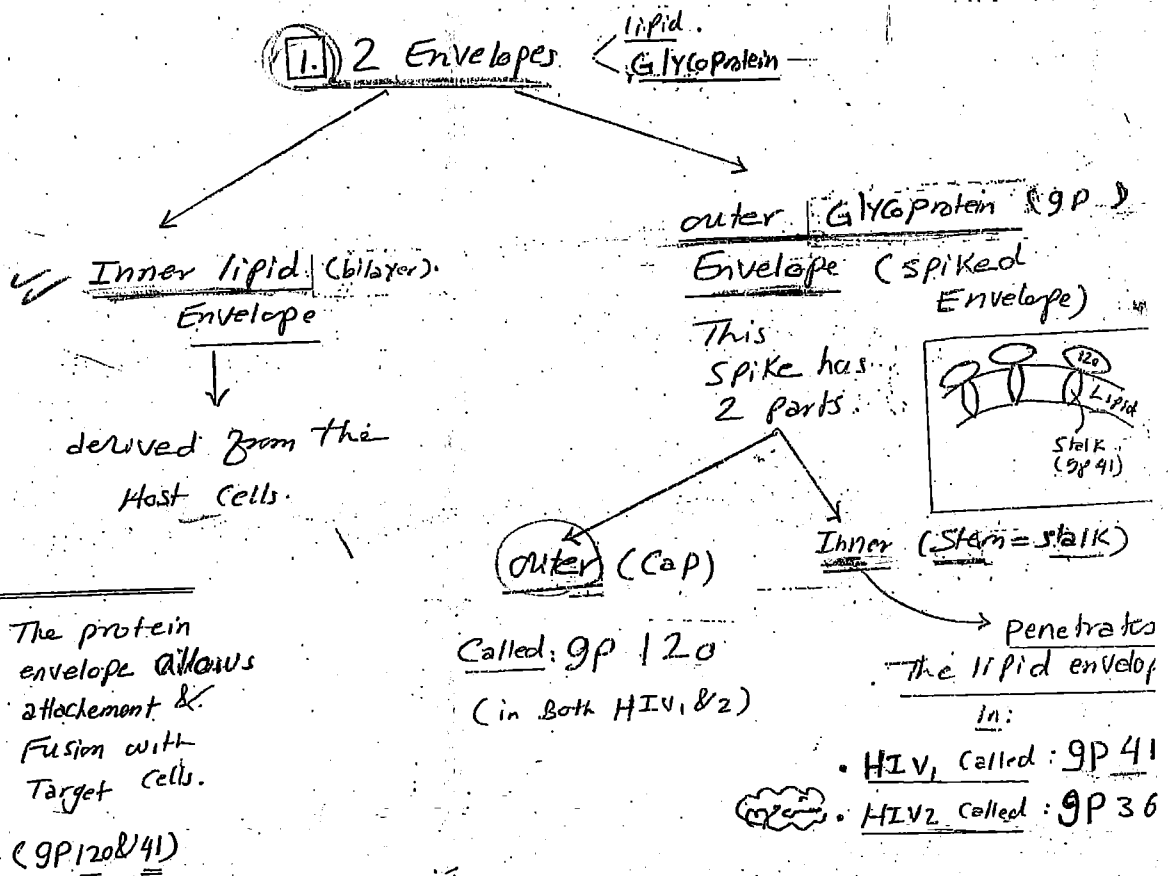


7.2 Replication of HIV within CD4⁺ lymphocyte and target sites of antiretroviral drugs. NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor. *Drugs are currently under development.

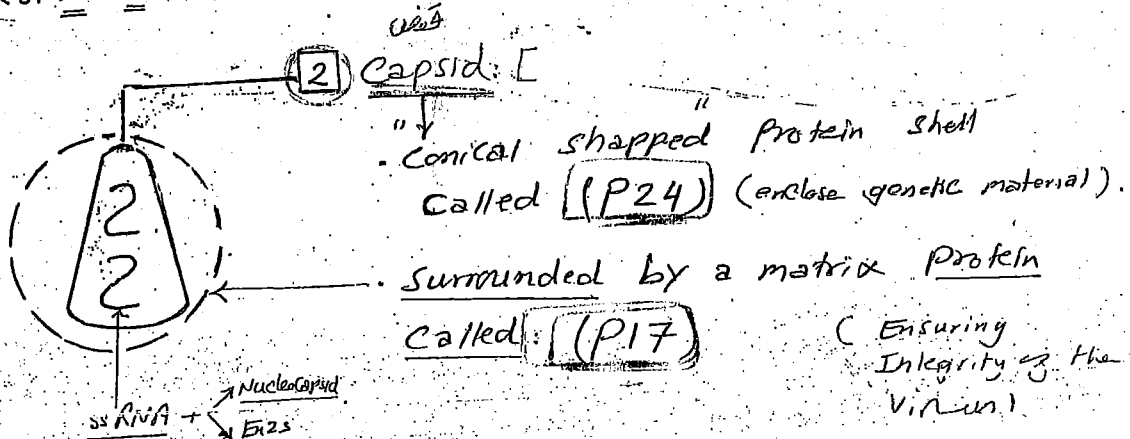
- ① Latency
- ② Persistent Viremia
- ③ Nervous System Inf.
- ④ weak host immune responses
- ⑤ High affinity For CD4 T cells & Monocytes.

Structure

A Molecular structure: Spike



MB: The protein envelope allows attachment & Fusion with Target cells.
(gp120/41)



(3) 2 RNA Copies (2 Single Strands):

Tightly bound to:

Nucleocapsid

Proteins:

. P6

. P7

. P9

Enzymes (RIP)

. Reverse Transcriptase

. Integrase

. Protease

Pathophysiology of HIV infection (Replication Cycle):

• Types of Targeted Cells:

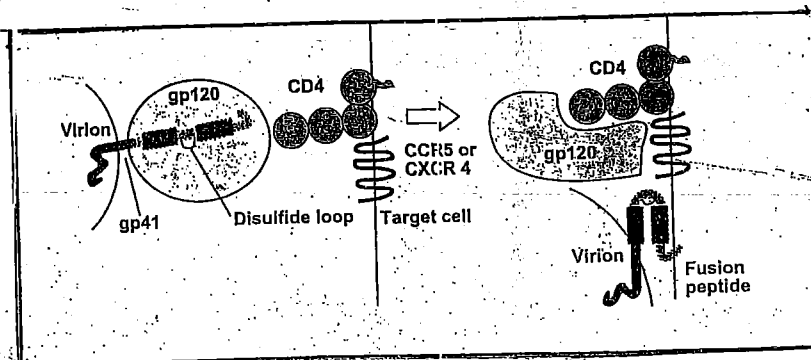
① CD4+ T Cells

② Macrophages

③ Dendritic cells

④ Microglial "

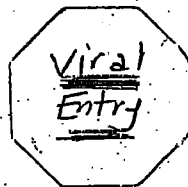
HIV disease is the most common cause of death among the infectious diseases.



Dr. M. Viral Replication Cycle

P. 5

- ① viral entry — $\left\{ \begin{array}{l} \text{attachment (Binding)} \\ \text{Fusion} \\ \text{uncoating \& entry} \end{array} \right.$
- ② provirus formation
- ③ provirus Integration
- ④ Transcription & Translation
- ⑤ viral Assembly
- ⑥ viral budding.



- ① Attachment (Binding): Attachment of viral proteins gp120 & gp41 to Target Cell receptors CD4 & Coreceptors $\left\{ \begin{array}{l} \text{CCR5} \\ \text{CXCR4} \end{array} \right.$

- ② Fusion: bet. the viral Envelope & Host-cell memb. (d.t. penetrate CM by gp41 \rightarrow Approx. 2 CMs \rightarrow Fusion).

genomic material
المادة الجينية
gp

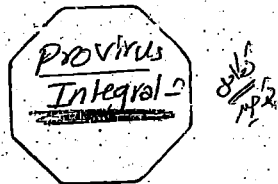
- ③ unCoating & Entry: virus is unCoated as it penetrates the cell \rightarrow release its genomic material into Host Cell cytoplasm.

& Leave it $\left\{ \begin{array}{l} \text{gp120 on Host} \\ \text{gp41 cell surface} \end{array} \right.$ (5-6%)

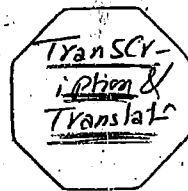


The enz. reverse Transcriptase makes Viral DNA (provirus) From The viral RNA.

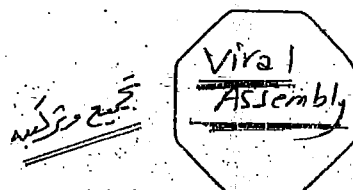
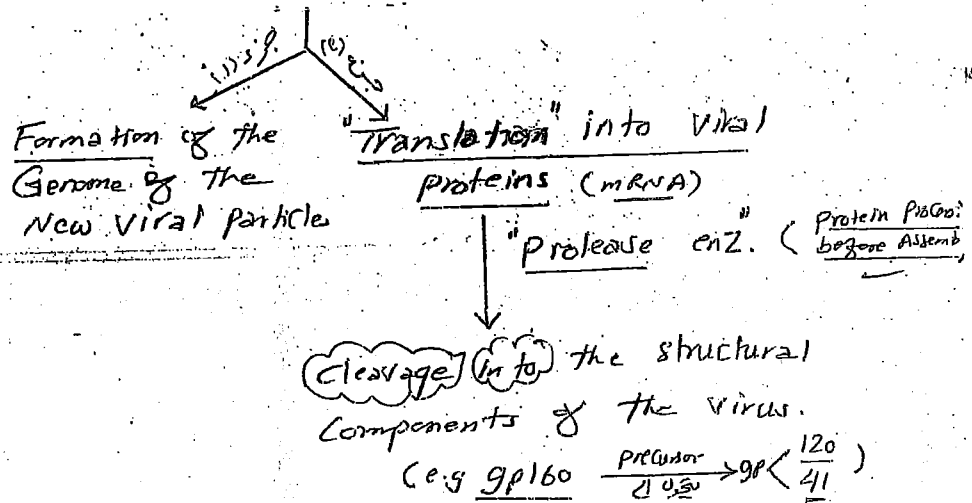
(ssRNA \rightarrow dsDNA)



The provirus enters the nucleus & become integrated to the Host DNA by the enz. "Integrase"



Transcription of Provirus DNA Into RNA.



The genomic RNA + viral proteins (enzs) → Assembled to Form intact Virions. (virus)

Viral Budding

Intact virus is released by "budding"
From the infected cells. (taking lipid Envelope from The Host Cells).

لا حظه
درای
خیزش
یویا
Marked Viral Mutate
Marked & CD4 +

Cellular death (CD4) Mechanism

1. Newly Formed virus & GP120 spikes → bind to adjacent CD4 → make holes → swelling & death.
2. The Host cells with surface proteins GP < $\frac{120}{40}$ will
 → recognized as foreign Ag → CD8 attack it → death.
 → Adhere to adjacent CD4 → Syncytium Formation (doz) → Syncytial cell death.

Syncytium
Plant or large cell like structure

after marked depletion of CD4 +
Macrophages become the
Source of HIV production.

قائمة سرية Types of HIV

HIV1	HIV2
<ul style="list-style-type: none"> • Originated From "Chimpanzee" • World wide • More virulent • Easily Transmitted • GP41 & Vif gene 	<ul style="list-style-type: none"> • Originated From "Sooty Mangabey" • Mainly West Africa • less virulent • less Transmissible • GP36 & Vif gene

فیل
سنگال

HIV₁ subtypes

(From A-G: ACC. to Geographic distribution)

Area	HIV ₁ subtype	Spread	Epidemiologic data
شمال أمريكا جنوب أوروبا أستراليا	B	Homosexuals Bisexuals IVD abusers	M:F (10:1) rare in infants
مصر وأفريقيا الكبرى الهند إيطاليا	ACD C B E	→ Heterosexuals as ↑ + IVDAs as ↑	All M:F = 1:1 Common infant infection

Epidemiology of HIV Inf: (2007): ✓

(i). Pandemic began on (1981)

(ii). 40 million of world's population is infected → 25 million deaths.

By HIV

> 90% infected in developing countries

> 5 million.

في أفريقيا

• أكثر المناطق انتشاراً :

(Subsaharan Africa)

→ Africa → 68.5% (25 million)

→ Asia → 14.5%

→ High income countries → 6.5%

→ Latin America → 5.5%

→ Eastern Europe → 4.5%

Since 1981 → 25 million deaths.

2005
14... حالة لوبيا
= 50 مليون
حالة م / سنة
3 مليون حالة
موتة
في سنة

Mode of Transmission:

① Sex: (70-80%): (Commonest Mode)

• Vaginal (60-70%): Major route of spread in Africa

• Anal (5-10%): } Major route of Transmission in Europe & USA

The presence of Mucosal Trauma & Genital ulceration
→ Facilitate the spread.

• Oral: → Very rare.

② Contaminated needles (5-10%) — ^{Inj.} Accid. (<0.01%)

- IVD Abs (IV drug Abusers).
- sharing needles.
- Injections.

③ Transfusion of Blood & Blood products Specially in hemophiliacs.

④ Mother to child Transmission: (MTC) (5-10%):

• Intrapartum (Commonest): through Contact with cervical & vaginal secretion.

Antepartum → • Transplacental: (In utero).
• Breast feeding.

Genital ulcers
&
HIV inf.
??
(See 5)

⑤ Organ & Tissue Transplantation & donation: e.g.

- Skin
- Kidney
- Corneas
- Semen
- BM
- Tendons

⑥ Accidental: among Health care workers: is extremely rare ($<0.01\%$) as Needle prick injury

NB: ① HIV: has been Isolated From all body Secretions

- as:
- | | | | | |
|------------|------------|----------|-------------|--------|
| • Semen | Secretions | • Tears | Lymphocytes | |
| • Cervical | | • urine | | Plasma |
| • CSF | | • saliva | | |

↓

& This doesn't mean that all can transmit the Inf. because concentration of virus in them varies considerably

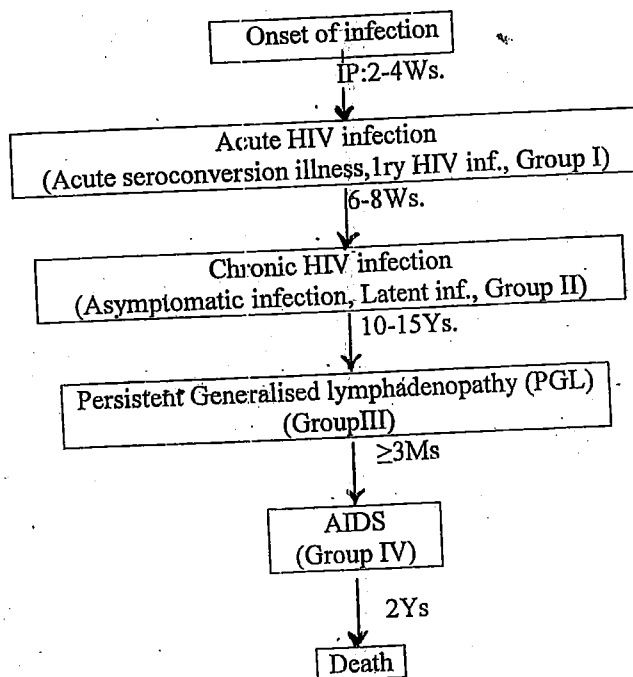
• The most infectious of them: (دقيق)

- Blood
 - Semen
 - Cervical Secretions

② There is no Evidence That: the virus is Transmitted By Causal or Social Contact: e.g.

- | | | |
|------------------|------|-------------|
| • Mosquitoes | Cups | |
| • Swimming pools | | • Toilets |
| | | • Air Spore |

CIP of HIV Inf; Natural History



So CIP of HIV Inf. (عبارة عن مراحل)

① Acute HIV infection (Acute seroconversion illness, 1ry HIV inf., Group I)

Def. Period between Exposure to the virus & full development of Antiviral Antibodies = (Window phase)
when antibody test becomes +ve for HIV

onset: 2-4 wks after inf. (IP of HIV) (2)

duration: 6-8 wks. (4)

Manifs: $\left\{ \begin{array}{l} \text{Asymptomatic in } \approx 30\% \\ \text{Symptomatic } \approx 70\% \rightarrow \text{Non specific} \\ \text{(Influenza like manifestations)} \end{array} \right.$

① General: F.A.H.M & L.N (Generalized)

② Hematological: Anemia & thrombocytopenia.

- 3 Neurological $\left\{ \begin{array}{l} \text{Neuropathy} \\ \text{Myelopathy} \end{array} \right.$
- 4 Dermatological: $\left\{ \begin{array}{l} \text{maculopapular rash at trunk} \\ \text{Reactivation of Shingles: (indicate Modest } \downarrow \text{ in Immunity)} \end{array} \right.$

5 Mucosal:
 "فجوة" Thrush d.t. Candida (Sign of Marked \downarrow in Immunity \rightarrow (CD4 200-500 Cells/ μ L))

Oral Hairy leukoplakia:
 (d.t. EBV.) \rightarrow Other Causes $\left\{ \begin{array}{l} \text{Behcet} \\ \text{ulcerative Colitis} \\ \text{HIV + Sero Neg.} \end{array} \right.$

HSV inf. (d.t. EBV.)

Aphthous ulcers of Post. Oropharynx.

Various white plaques at side of tongue can't be rubbed off.

Hairy: N. white with Hairy on shaggy like.

Events:
 Viral load \rightarrow Peak $\uparrow\uparrow$ (Most sensitive for β)
 CD4 Count \rightarrow Peak $\downarrow\downarrow$
 P24 Ag \rightarrow +ve (...)
 Antibodies $\left\{ \begin{array}{l} \text{Anti P24} \\ \text{Anti gp41} \end{array} \right. \rightarrow$ -ve (Window phase)

أحداث

تعبئة
 • Viral load & CD4 Count
 • P24 & Anti P24

CIP

Definition
 Onset
 Duration
 Manifestations
 Events:
 - Viral load
 - CD4 count
 - P24 Ag
 - Antibodies (Anti p24 and gp41)

2) Chronic HIV infection
(Asymptomatic infection, Latent inf., Group II)

P. 13

Onset: With Full development of Antiviral Antibodies (after Termination of Acute Seroconversion illness).

duration: 10-15 Ys. (then AIDS)

manifestations: → Asymptomatic (but some patients having persistent Generalized L-N (PGL))

Events:

Viral loads: ↓↓ [to its lowest point (Viral set point) & persist at relatively steady state] d.t. efficient Immunity (Abs)

CD4 Count: Progressive steady ↓↓ (50 cells/mm³)

✓ P24 Ag: -ve
✓ Antibodies $\left\{ \begin{array}{l} \text{Anti-P24} \rightarrow +ve \\ \text{Anti-gp41} \rightarrow +ve \end{array} \right.$ (only +ve → always +ve)

3) Persistent Generalised lymphadenopathy (PGL)
(Group III)

onset: during The Asympt. stage. Cdt affects some pts

duration: till onset of AIDS (≥ 3 ms)

Manifs: Generalised L-N That's Ch. by

→ L-N > 1 cm in diameter

→ ≥ 2 Extragnathal sites

→ ≥ 3 ms duration

→ Not d.t. Any other Cause.

Events: Viral load, CD4 & Anti gp 41 → as Asympt. inf.

✓ P24 → start to be +ve

✓ Anti P24 → " " -ve

[Bad Prognosis]
AIDS (if +ve)

PGL

• May be the presenting Feature of

HIV
SI Inf

• may be a clue that the patient will progress to AIDS

Definition: End stage of HIV disease that, \checkmark ch BY Δ :

- $CD4 < 200$
- opportunistic Inf.
- Malignancy.

• onset: 10-15 y^s from onset of inf.

• duration: \approx 2 y^s (then death).

• Manifestations:

General
inf.
malignancies

(A) General Manif.: \leftarrow ARC \leftarrow HIV Encephalopathy

(I) Constitutional Manif. (AIDS related Complex = chr. Fatigue syndrome) [ARC]:

mild prodromal manif. in HIV patient

that may precede the appearance of

Full-blown AIDS & its serious manif.

Diagnosis of ARC, (≥ 2 clinical + ≥ 2 lab).

أسباب

1. Clinical:

2. Lab.:

Causes of Death in AIDS

1. Opportunistic Inf.
2. Wasting
3. Encephalopathy
4. My (less common)

• Fever $\geq 38^{\circ}C$

• diarrhoea

• w.t loss $\geq 10\%$ of BSA

• Skin Rash (Maculopap.)

• HZ (Multidermatomal)

• OHL. Oral Hairy leukoplakia

• oropharyngeal candidiasis.

• $CD4 < 400$ (in AIDS < 200)

• \uparrow Igs (in " $\rightarrow \downarrow \downarrow$)

• Follicular or mixed

Hyperplasia of L.N (in AIDS
 \downarrow
degen.)

(II) Neurologic dis. (HIV encephalopathy)

if / $\frac{\text{oral Candidiasis (Thrush)}}{\text{OHL}} \rightarrow \text{AIDS } \bar{e} \text{ in } 6-12 \text{ ms.}$

العدوى المنزلة إلى كبد في مرضى AIDS ← "خبيثة"

(A) opportunistic Inf.

1. Bacterial:

• Mycobact:

• TB (Extrapulm.) - HAIC
• Atypical MYCb. - M. Kaposi (disseminated)

• Salmonella: Recurrent bacteraemia.

2. Viral:

• HSV: chr. mucocut. (>1m) or disseminated

• VZV: Recurrent, Multidermatomal.

• EBV: OHL • CMV: infects

John Cunningham Virus → JC Virus ← PML: Progressive multifocal leukoencephalopathy. [Fetal viral dis chr & y. progressive damage of white matter of brain]

3. Fungal: (cm)

• Candidiasis (Thrush): Esophagus, Trachea & bronchi.

• Cryptococcosis: (Extrapulm.).

• Histoplasmosis: (disseminated).

Pneumocystis Carinii
Pneumonia.
Cryptosporidiosis
(= chr. diarrhoea >1m)
Toxoplasmosis of
Brain.

4. Parasitic: Strongyloidiasis (Extraintestinal)

5. Protozoal:

(B) Malignancies:

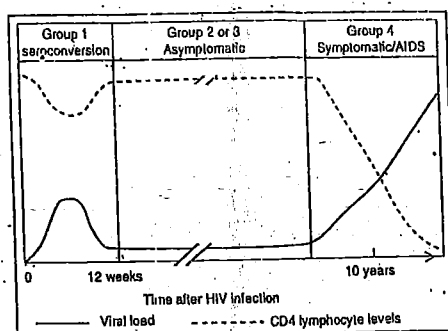
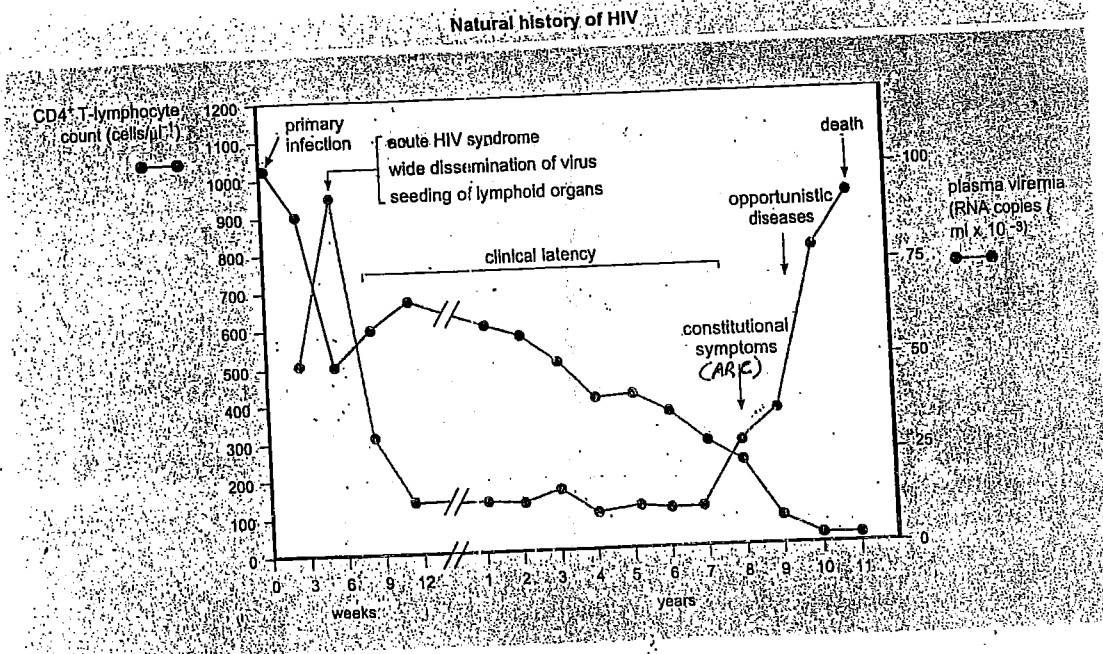
• Kaposi Sarcoma.

• Lymphoma (non Hodgkins & dry lymphoma of the brain).

Events:

- Viral load: Very High $\uparrow\uparrow$
- CD4+ Count: Very low $\downarrow\downarrow < 200$
- P24 Ag $\rightarrow +ve$
- Antibodies
 - Anti P24 $\rightarrow -ve$
 - Anti gp41 $\rightarrow +ve$

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Association between virological, immunological & clinical events
& time course of HIV infection.

CDC classification (Staging) of HIV

① CDC 1992 :

Table 22.6: CDC classification of HIV disease (1992)

Group I	: Primary HIV Infection (Acute Seroconversion)
Group II	: Asymptomatic Infection (Latency)
Group III	: Generalised lymphadenopathy (PAL)
Group IV	: AIDS
Subgroup A	: Constitutional disease (ARC) & HIV wasting Synd. (Slim)
Subgroup B	: Neurologic disease (HIV Encephalopathy)
Subgroup C	: Secondary infectious disease (Opportunistic inf.)
Subgroup D	: Secondary Cancers Kaposi's sarcoma Non-Hodgkins lymphoma Primary lymphoma of the brain
Subgroup E	: Others

② CDC 1993: جدول

CDC 1993 classification system for HIV disease			
	(1)	(2)	(3)
CD4 lymphocyte count $\times 10^6/l$	>500	200-499	<199
A) Asymptomatic including groups I, II and III	A1	A2	A3
B) Symptomatic (Not A or C)	B1	B2	B3
C) AIDS-defining conditions	C1	C2	C3

- dis. d.f. ↓↓
GME or
Complicated
BY HIV
inf.

Opportunistic
inf.

- ① = Asymptomatic
- ② = Symptomatic = diarrhoea, fever, candida, ...
(Not manifs. of seroconv. or AIDS)
- ③ = AIDS: A3, B3, C1, C2, C3.

Laboratory Dx of HIV "Up.PP"

P-18

- ① Viral Load
- ② Viral Culture
- ③ Viral Antigen
- ④ Antiviral Antibodies
- ⑤ Others

1. Viral load Assessment:

- Methods:
- ① RT-PCR test (Reverse transcriptase PCR)
 - ② bDNA test (branched DNA)
 - ③ NASBA (Nucleic acid sequence based Assay)
- Advantage

①

Diagnosis of

Early Inf.

Late Inf.

Ab⁺ / High

Ab⁺ / High

Highly Sensitive
detect even non
Replicating
virus.

① Early Inf.: during window phase (it detect window phase to ≈ 12 d)

② Infants of HIV mother.

③ Late Inf.: when there is False -ve

ELISA & WB (d.f. severe immunodeficiency)

Antibodies (high level)
(False -ve)

Very

② Assessment of dis. Progression (Viral load)

- Acute seroconversion \rightarrow \uparrow load
- Asymptomatic inf \rightarrow \downarrow Load (set point)
in 6 mo of inf.
- (AIDS) Symptomatic inf \rightarrow \uparrow Load.

③ Assessment of HIV Efficacy:

If with HIV RNA

↓ 30-100 Fold ↓ in viral load.

↓ ↓ e in 1w

Good response

↑ ↑

emergency drug resistance.

- disadv. - ① Sensitive but non specific.
② Not yet standardized.

↓
⑤ Not used as a diagnostic tool.

② Viral Culture:

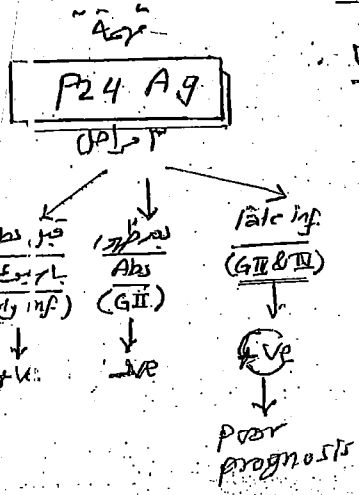
Source (MHV) ← Peripheral Blood Lymphocytes (PBL)
CSF.
Tissues

Adv. → Most specific (ultimate diagnosis)

disadv. → • difficult
• Expensive
• Not for routine use.

③ Viral Antigens (P24 detection):

Method: Monoclonal Antibody



- Value: ① Diagnosis → early diagnosis of Inf. before AntiViral Antibs. (Seroconversion illness).
② Prognosis → reappearances after disappearance → Bad prognosis (Late Inf.)

③ Assessment of HIV Efficacy

disadv. (1) low sensitivity (Fluctuation in level)

(2) Not yet standardized.

تم ايجتهاد
بالتفصيل
(HIV RNA PCR)

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4

Anti viral Antibodies:

3 Abs. Anti $\left\{ \begin{array}{l} \text{p24} \\ \text{gp41} \\ \text{gp120 \& 160} \end{array} \right.$

3 detection technique $\left\{ \begin{array}{l} \text{ELISA} \\ \text{WB} \\ \text{RIPA} \end{array} \right.$

لا يتم تفريقه \rightarrow Fluctuation (physiology of Anti HIV)

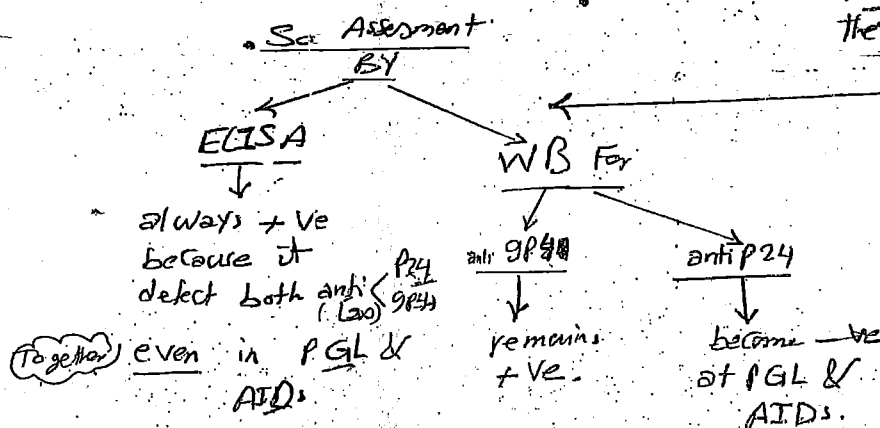
① onset & appearance: Immediately after
Inf. & during Acute seroconversion illness the
Antibodies can't be detected & this
Period of -ve Antibodies called

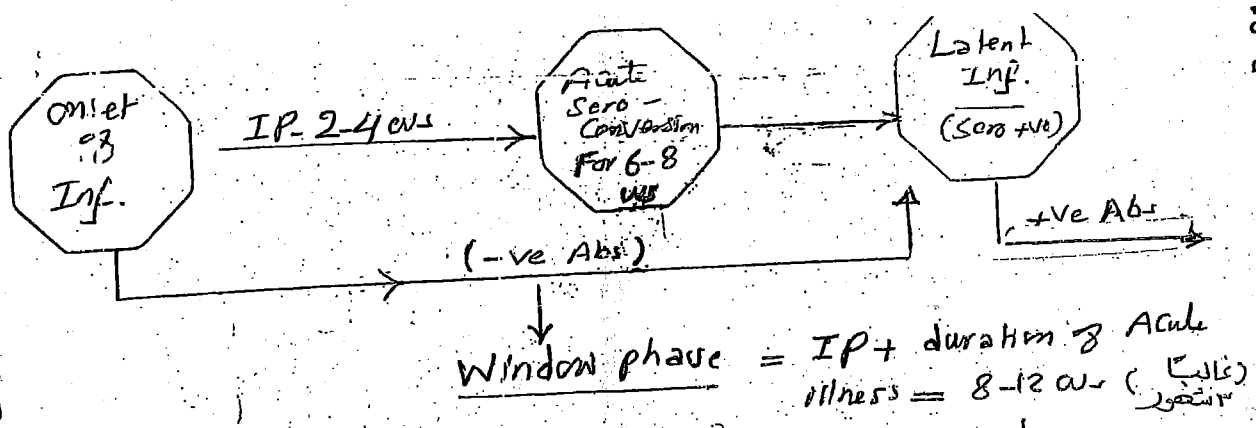
"Window phase" (3 wks - 6 mos)

So Antibody
Tests are
(False -ve)

- usually: 3 mos $\xrightarrow{\text{then}}$ Sero +ve
- Most cases (99%) \rightarrow are Sero +ve at 6 mos
- 12 ms window phase: may occur e H in
ART or HCV.

② once they are +ve, Anti $\left\{ \begin{array}{l} \text{gp41} \rightarrow \text{remains +ve} \\ \text{p24} \rightarrow \text{remains +ve} \end{array} \right.$
Except at
PGL & AIDS \rightarrow
they are (-ve)





A. ELISA

-ve Abs

دائماً +ve →
Always +ve.

- detect Antibodies Against the whole viral proteins (P24, gp41 & gp120)
- Ch-by ① Sensitive (Good -ve Test)
- ② Non Specific (False +ve)

So it's: The most widely test used for screening of Blood donors.

HIV + HCV
(التهاب الكبد)

False +ve in
 Blood Mg
 MM
 BPC
 DNA viral inf. (HCV)

B. Western Blot

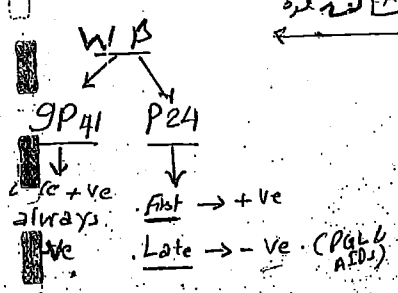
(يستخدم للتحقق من نتائج اختبار ELISA)
Viral Proteins

- detect Antibodies against certain single specific viral protein (purified HIV proteins used)

النتيجة تكون

- as:
- P24
 - gp41
 - gp120/160

لا يتم اختبارنا لنقول انه
اجمالي يكونه في
خبره فيكونه مع البروتينات
(من نوع واحد فقط)



Specific (Confirm & Rules out false +ve ELISA)

RIPA

Radio ImmunoPrecipitation Assay.

Adv: clarify atypical or Indeterminate WB

disadv: not yet standardized.

لوجالک مریض (أو عیلة دم) وشاکن انه (HIV)
 ها نقلنا لده

سوال برقی

ELISA (Rapid Screening)

- Ve (non Reactive)

مریض نیست

+ Ve

Repeat the test

still + Ve

Confirm

W.B (For Abs against 2 protein substrates)

- Ve

مریض نیست

+ Ve

HIV

Indeterminate

either

Repeat WB

بعد ۲-۳ هفته

or

RIPA

(عمل ایمنی)

5 → Other Investigation: (see the table)

P. 23

Table 22.11: Other tests to be performed in AIDS

1. Hemoglobin concentration
2. Total and differential leukocyte counts
3. Quantitation of CD4 and CD8 lymphocytes
4. Platelet counts
5. Serologic tests for syphilis
6. β -microglobulin level
7. Hepatitis B and toxoplasma serology
8. Skin tests for tuberculosis and one or more control antigens
9. Skiagram of the chest

ES
Tuberculin

IB: Total Leucocyte Count: 4000 - 11000 /mm³

Lymphocytes: 15-45% of TWBCs (\approx 1000 - 4800)

↓
CD4 → 30-60% (500-1500)

CD8 → 20-40%

B Cells → 5-20%

- IB

- leucocyte count

- CD4, CD8 lymphocyte

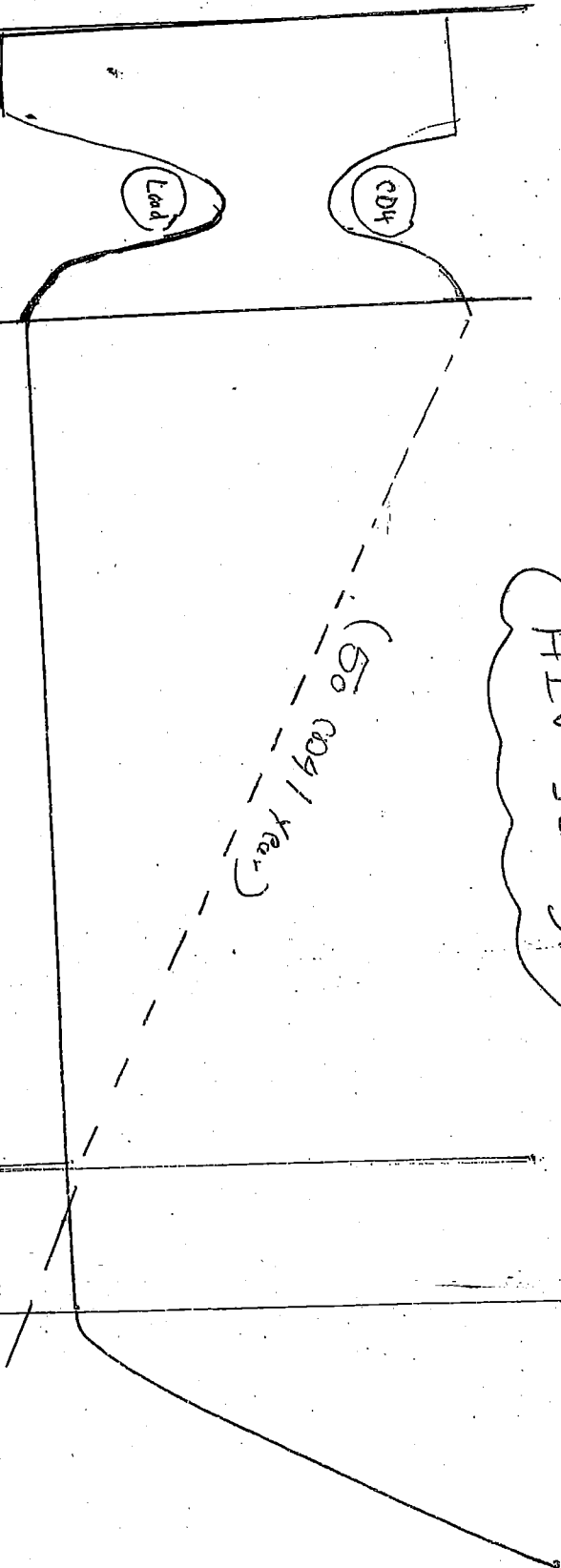
- pH

- S

- HBV

HIV Serology

500
500



(50% (0.5 / Year))

death

GI (Acute)

GII (Asympt.)

GIII (DGL)

GIV (ADL)

Load

Peak M (Transient)

Rapid W (11)

± ve

- ve

Window phase

Steady (Viral set point)

Steady ↓ (Seroconversion)

- ve

+ ve

+ ve

+ ve

↓ W-ve

- ve

+ ve

↑

↓

↓

↓

↓

↓

علامات و درج HIV

علامت . Markers of dis. progression: ✓

1. Lab:

- High viral load
- low CD4 Count
- appearance of P24 & disappearance of P24 Abs.

2. Clinical:

- Fever
- diarrhea
- Wt loss
- oral Candidiasis
- oral H.L.
- H-Zoster.

نکته ✓ Patients who need close monitoring: X

- $CD4 < 350$
- Rapid ↓ CD4
- ↑ viral load
- Severe symptoms → Candidate for HAART.

HIV in children (Age < 13 Ys)

P. 26

Route of Inf (MTCT)

- Transplacental (in utero)
- Intrapartum (by cervical & vaginal secretion) →
- Breast Feeding (±)

Commonest
85%

Incid : (30%) of Infants born to HIV Infected mother will be infected either Transplacentally or Commonly Intrapartum.

Diagnosis:

- ① HIV Ab (IgG) → مقاومة فيروس نقص المناعة
- ② P24 Ag → may be obscured by maternal Antibodies.
- ③ Viral Culture or Nucleic acid detection by PCR

Follow up

• 36-48 hrs after delivery (not Cord Blood)

Then • 3-4 wks

Then • 3 mo Interval

(by)

Assessment of

- P24
- Abs
- Viral load.

CDC 1994 Revised Criteria
For children < 13 y

P. 27

Category N: → No Symptoms

Category A: → mild symptoms.

- L.N
- HSM
- Dermatitis
- Parotitis
- URTI (Recurrent)

Category B: → moderately sympt.

- Fever
- diarrhoea > 1 m.
- Pancytopenia
- Bacterial → pneumonia
- Viral → Herpes Stomatitis & Varicella
- Candidal → oropharyngeal
- Cardiomyopathy & Hepatitis

LIP

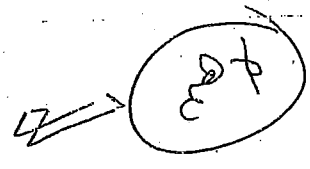
↓
Lymphocytic
Interstitial
Pneumonia

Category C: → Severe Symptoms.

↓
AIDS criteria

(LIP) → criteria

Clinical differences bet Childhood & Adult HIV



- more rapid progression
- Higher viral load
- Higher absolute CD4 count
- Common $\left\{ \begin{array}{l} \text{Growth Faltering (of Height & Wt.)} \\ \text{LIP (Lymphocytic Interstitial Pneum.)} \end{array} \right.$
- un-common Mg
- Opportunistic Inf. \rightarrow encountered for the 1st time (1st illness may be \searrow severe than opportunistic inf in adults).

More Rapid clearance of HAART \rightarrow So they require higher doses than adult Equivalent doses.
needed.

* Management:

- Triple HAART
- Antibiotics
- Good Nutrition
- IVIG
- LIP \rightarrow CS²
- Prophylaxis \rightarrow P. Carinii & Fungal Inf.

Treatment of HIV disease

P. 29

- ① prevention strategies
- ② Vaccines
- ③ Antivirals
- ④ Immunostimulants
- ⑤ opportunistic Inf. H.

① Prevention Strategies:

A. Health Education

Knowledge of Transmission routes.

Risk reduction strategies e.g. Condom

Sexual health education in schools.

B. Sex → "Safe Sex"

• avoid sex (only sure prevention)

• Avoid sex with many partners

• Condom use.

C. Blood & Blood products Transmission:

• Avoid High Risk donation.

• Screen Blood for HIV.

• Heat H for Individual Blood products.

D. IVDA's : Avoid < Injection Sharing the injecting equipments.

E. Vertical transmission:

• Contraception → for Sexive women.

Pregnancy:
doesn't worsen
the
distal
prognosis

termination : ...

Antepartum

start as early as possible (14 wks)

Intrapartum

vaginal delivery (منزلاً)
Body Isolate of fetus,
Washing thoroughly

Post partum

avoid $\left\{ \begin{array}{l} \text{lactate} \\ \text{IUCD} \end{array} \right.$ (# inf.)

Mother loading dose

منزلاً

+
of

Fetus: Early #
from birth to 6 wks.

② Vaccines : A. difficult to develop why??

- unknown Immune response that protect from it.
- May enhance Inf.
- greater diversity in viral genome.
- Trials needs much $\left\{ \begin{array}{l} \text{Time} \\ \text{Cost} \\ \text{pt.} \end{array} \right.$

B. Vaccines under trial:

1. Subunit Vaccines.
2. live recombinant Micro-organisms
3. passive Immunization for short period.

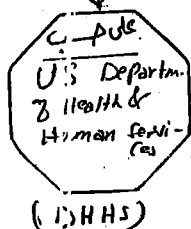
③ Antiviral treatment (HAART)

Highly active Antiretroviral therapy.

✓ Principles:

1. Monitor $\left\{ \begin{array}{l} \text{CD4} \\ \text{viral load} \end{array} \right.$
2. Early # before Immunodef. become apparent
3. ↓ viral load as much as possible (for) as long as possible.
4. use combination (معاً)

Indications for Duration of HAART:



1. Any Pt with $\left\{ \begin{array}{l} \text{AIDS defining illness or} \\ \text{Severe symptoms of HIV} \\ \text{inf.} \end{array} \right.$

regardless CD4 count.

2. Any patient with $\left\{ \begin{array}{l} \text{CD4} < 200 \text{ /mm}^3 \\ \text{viral load} > 100,000 \text{ Copies/mL} \end{array} \right.$

Regardless Symptomatic or Asymptomatic.

3. Prevention of Vertical transmission:

• علاج الأم \leftarrow قبل الولادة 4-6 أسابيع [loading dose AZT]

• من الولادة لمدة 4 أسابيع: علاج الولد [AZT IV]

Lamivudine (300d)

Zidovudine (600d) +

Indinavir (800x3d) +

(LZC)

علاج (3Combinat)

4. Post Exposure Prophylaxis (PEP)

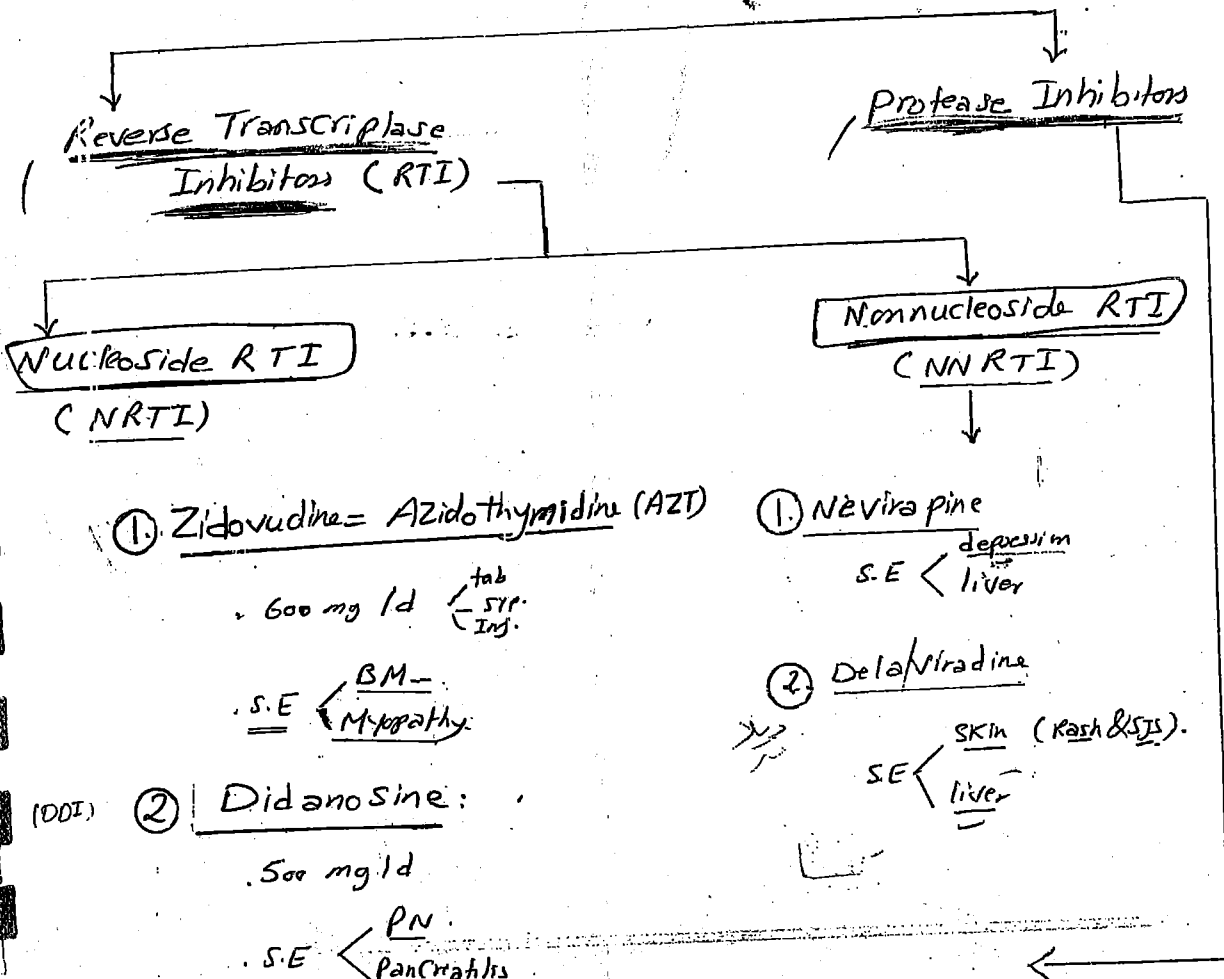
Indications to change:

- ① Failed drug $\left\{ \begin{array}{l} \text{Fever, wasting, opportunistic inf.} \\ \uparrow 3 \text{ fold viral load.} \\ \downarrow \text{CD4.} \end{array} \right.$
- ② Drug \rightarrow Toxicity & Interaction.
- ③ Monotherapy \rightarrow Multitherapy.

Indications For combinations:

- ① Resistant
② Improved survival
③ ↑ Efficacy.

HIV ART.
2 Inhibitors → Reverse Transcriptase Enz.
Protease Enz.



① Zidovudine = AZidoThymidine (AZT)
 . 600 mg 1d $\begin{cases} \text{tab} \\ \text{Syr.} \\ \text{Inj.} \end{cases}$
 . S.E $\begin{cases} \text{BM-} \\ \text{Myopathy} \end{cases}$

(DDI) ② Didanosine:
 . 500 mg 1d
 . S.E $\begin{cases} \text{PN} \\ \text{Pancreatitis} \end{cases}$

(DDI) ③ Zalcitabine:
 . 1-5 mg 1d
 . S.E $\begin{cases} \text{PN} \\ \text{Pancreatitis} \\ \text{GIT ulceratn.} \end{cases}$

① Nevirapine
 S.E $\begin{cases} \text{depression} \\ \text{liver} \end{cases}$
 ② Delaviradine
 SE $\begin{cases} \text{SKIN (Rash \& SJS)} \\ \text{liver} \end{cases}$

SIR
 ③ $\begin{cases} \text{Saquinavir (600 mg X 2/d)} \\ \text{Indinavir (800 X 3/d)} \\ \text{Ritonavir (600 X 2/d)} \end{cases}$

S.E $\begin{cases} \text{Saquinavir} \rightarrow \text{No S.E} \\ \text{Indinavir} \rightarrow \text{Renal stones \& } \uparrow \text{Bilirubin} \\ \text{Ritona} \end{cases}$
 V.GIT
 Liver
 DE

NBS
 . NRTI: Faulty Blocks or Pieces when incorporated to DNA → chain terminal
 . NNRTI: -- RT enzyme.

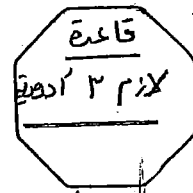
NB. Both Reverse Transcriptase Inhibitors Nucleoside
Non Nucleoside

inhibit RT Enzyme but by different mechanisms.

→ This allow: ① ↑ efficacy ✓
② ↓ resistance ✓
③ ↓ Toxicity ✓

Triple Therapy: usually used:

• 2NRTIs + 1PI
or • 2NRTIs + 1NNRTI.



Other Antivirals (see steps of Viral Replication).

① Entry Inhibitors:

(Gp120/CCR5) ← Binding inhibitors → Maraviroc (CCR blocker)
(gp41 Penetrator) ← Fusion → Enfuvirtide
Uncoating → Etravirine.

② Integrase Inhibitors: Elvitegravir.

③ Transcription & Translation Inhibitors:

Tat Inhibitors
Antisense Constructs
Ribavirin

④ Viral Budding Inhibitors:

Interferon ✓
Antibodies
Ligands.

⑤ Natural Inhibitors:

← Ceftriaxone (Vitecon) ← causing defect of capsid p24 protein at viral replication & assembly

⑥ Broad Spectrum Inhibitors

Mushroom Extract

USD HHS

لو فاحصه حامل - وعندها HIV
طريقة الولادة ؟؟

C.S Preferred if.

Vaginal preferred if.

didn't Receive Prenatal Care

ANY HAART

Viral load > 1000 Copies/ml.

Received Prenatal care
Viral load < 1000 Copies/ml

في كل الكالسيوم قبل الولادة

- ① IV AZT : 3 hrs before labor
- ② IV AZT : during labor

③ ↓ Fetal Exposure to mother's blood &
avoid Forceps Vacuum.

④ IV AZT For Fetus From
birth to 6 wks.

Human Herpes Virus group

As in dermat.

P. 35

Herpes: Greek word means "To creep or crawl" in reference to the spreading nature of the dis.

Herpetiform: lesion that is similar to HSV (multiple grouped vesicles on erythematous base or similar to Herpetiform ulcer). Circular, superficial Erosion

Human Herpes Virus group char:

①. double stranded DNA

②. Replicate intranuclear.

③. produce: 1st infect → at site of inoculat

Latency → in Nervous or Lymphoid Tissues.

Reactivated & Recurr. inf. in later life either spont. or ppt. agents.

Classification of Human herpes viruses "HHVs"

HHV 1 Skin & oral mucosa → H. labialis.

HHV 2 Genital areas → genital herpes.

HHV 3 Varicella zoster.

HHV 4 Epstein-Barr virus.

HHV 5 Cytomegalovirus

HHV 6 Exanthem subitum (roseola infantum).

HHV 7 Associated with roseola.

HHV 8 Associated with KS, Lymphoma. "onco-genic virus"

2 Ass

	HHV	Site of latency	Manifestations	
α-HV	HHV1 (HSV1)	Nervous syst. "Neurons"	H. labialis	1 st & recur-
	HHV2 (HSV2)		Genital herpes	rent
	HHV3 (VZV)		Chicken pox	1 st
			H. zoster	2 nd
β-HV	HHV5 (CMV)	Immune syst. "Lymphoid tissue"	Asympt. mono-like	
	HHV6		Roseola infantum	✓
	HHV7		Associated with Roseola	✓
γ-HV	HHV4 (EBV)		Infectious mononucleosis	
	HHV8		KS associated herpes virus	

for 5-10

Herpes Simplex Viruses

(HSV1 & HSV2)

Non genital H.S.V
usually affect non
genital skin & MM.

Genital HSV
usually affect Genital
skin & MM.

Herpes labialis
(Above waist inf.)

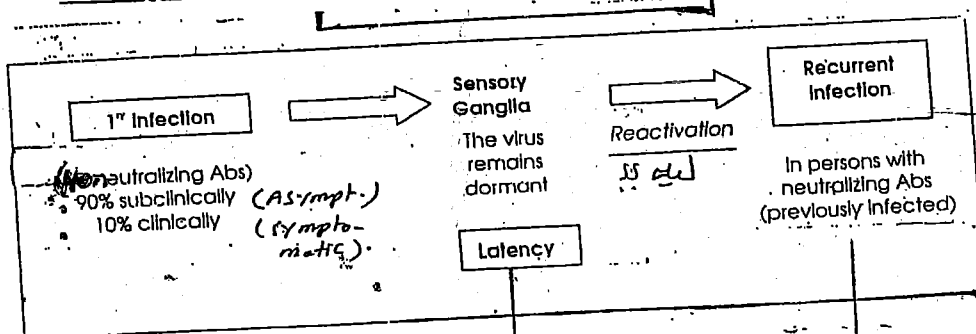
Herpes Genitalis
(Below waist inf.)

NB Nowadays HSV1 may affect the Genitalia (10-40%)
& HSV2 may affect non Genital skin & MM
(d.t. Common practice of oral sex).

Mode of Transmission:

- ① droplet inf. (in HSV1 labialis)
- ② Contact with active lesions (vesicular lesions before crusts) & infected secretions.
- ③ Sexually Transmitted (HSV1 & HSV2)
- ④ Vertical Transmission (From mother → Fetus)

Pathogenesis:



So may reinfected:

face
oropharyngeal MM
ocular MM.

Site of Latency

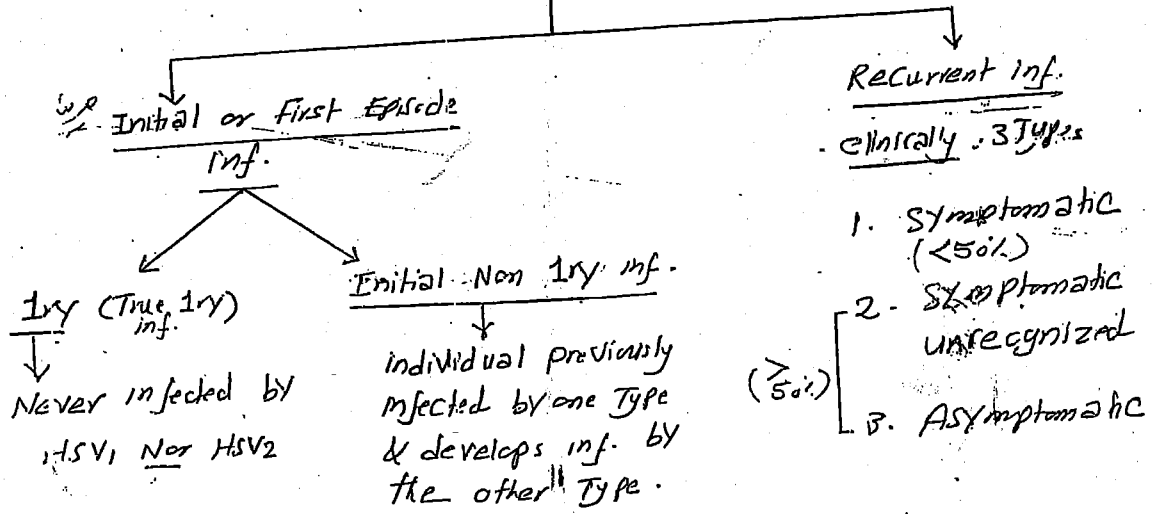
HSV1 Trigeminal Ganglion
HSV2 Lumbo-Sacral Ganglion
(L-L)
(hips, buttocks, genitalia)

Comment on:

incid. of recurrence
No. of recurrences
CIP of "

Types of Inf. Caused By

HSV



Clinically: 10% Sympt. & 90% Asymptomatic

Recurrent infection

- Causes of reactivation
- Incid.
- No of Recurrences/Y.
- CIP.

Causes of Recurrence: either

① Spontaneous

or ② predisp. factors

- Stress
- Sex
- Menses

- Fatigue
- Fever

- UVB (HSV1)
- Immune-suppression

Summed up to 50% recurrent HSV due to predisp. factors

Recurrence	HSV1	HSV2
• Cause		
• Incid.	≈ 50%	≈ 90%
• No of Episodes	≈ 1 / year	≈ 6 / year

So HSV2 recurs more common & more frequent > HSV1

Types of Recurrent inf.

1. Symptomatic: classical lesions & symptoms of HSV.
2. Asymptomatic: the virus descends from the dorsal routes along the nerve (no S. ners) (subclinical) & replicate at skin surface or MM without producing lesions or symptoms.
3. Symptomatic Unrecognized: المرض يكون سرطانيات سرية احمر - ارشكوى مع جلد ومن يعرف ان HSV الا لا يعرف كيف (non classical S & S of HSV inf.)

so that periods of Transmission or shedding of the virus may occur during:

- less common period of Transmission. ← 1. Symptomatic shedding: shedding during active symptomatic lesions.
- The Main & The Most important periods of Transmission. ← 2. Asymptomatic shedding: shedding during absence of clinical lesions. (the virus descend along the nerve → replicate & out-producing lesions).
3. Unrecognized shedding: المرض يكون سرطانيات سرية احمر - ارشكوى مع جلد ومن يعرف ان HSV الا لا يعرف كيف.

Diseases Caused by HSV:

1. 2 main diseases:
 - Oral labial H.S (H. labialis or facialis)
 - Genital H.S (H. genitalis or pro genitalis)

2. Other Herpetic inf:

- * Ocular H.S
- * Neonatal H.S
- * Herpetic whitlow
- * Herpetic Symples.
- * H. Gliadialorum

* Eczema Herpeticum

1. H. Encephalitis

* Herpes in Special situations

HIV

Immuno-Compromised.

Oral labial H.S (Commonest HSV inf.)

① Viral Transmission
 • HSV 1
 • HSV 2
 IP: 3-7 dr.

Primary infection → (Herpetic Gingivostomatitis)
 (MN)

10% Symptomatic
 90% Asymptomatic

△ Prothromal (marked) < Systemic: FAHM, L.N (+tender)
 Local: discomfort, burning, Tingling, Numbness & Tenderness.

△ Eruption (lesion): presentation acc. to age:
 • Vesicles: No. Grouping: [Gingivostomatitis: in children. → 3 Sites: oral, pharynx, gingivae.
 • Pharyngitis: in young adults.]
 • more numerous, Less grouped vesicles on erythema.
 base → rupture → crusts. 2-3 w. Resolute.
 Healing → 2-3 w.

Latency (in Trigeminal Ganglion)

Predisposing Factors For Recurrence
 Specially UVB (sun.)

Reactivation

Recurrent episode. → (Cold sore, Fever blister)

NB
 al skin Vesicle
 dome shaped
 umbilicated.

- prothromal as in 1st inf. but less marked
 Neutralising AB as in 1st
- Eruption (lesion): fewer No. of vesicles + marked grouping.
 Healing in 1-2 w.

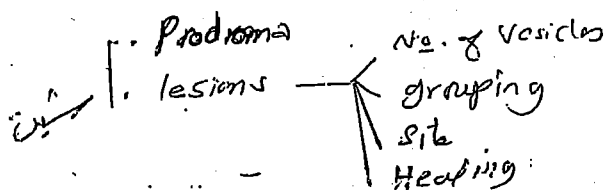
- Site of Lesions: Common lip (Vermilion border)
 Less Common

No MM affect

- perioral
- perinasal
- cheek
- ear lobule

d) Recurrence: $\approx 1/\text{year}$.

Note the difference bet. 1st inf. & Recurrent inf.



- Note that
- 1st orolabial H.S. : Called Herpesic Ganglionostomatitis
 - Recurrent " " : Called

2nd orolabial Cold Sore = Fever blister

- what is the common predisposing Agent? Sun (UVB).

1 st infection	Recurrent infection.
<p>IP: 3-7 days</p> <p>usually: Children or young adults (1-5%)</p> <p>usually: Asymptomatic & if symptomatic it will be more severe.</p> <p>Prodroma: Marked</p> <p>Exanthem: (lesion)</p> <p>①. more numerous vesicles & lesser grouping.</p> <p>②. MM: usually affected</p> <p>③. Healing: 2-3 weeks</p>	<p>Reactivation either Spont. or under effect of certain Agents.</p> <p>Adults.</p> <p>Symptomatic & less severe.</p> <p>Less marked</p> <p>Fewer vesicles & more grouping</p> <p>usually (not) affect the MM.</p> <p>lesion affect the same Region but not the exact area</p> <p>Healing 1-2 weeks</p>

Genital Herpes (Herpes progenitalis)

Def. infection of Genitalia by HSV.

AET & Transmission:

HSV₂ (70%) → Sexual intercourse.

HSV₁ (30%) → oral sex.

Types of infection:

1. True primary inf.
2. Initial non primary inf.
3. Recurrent inf.

Periods of Transmission: ± during

1. Symptomatic inf.

Most cases → 2. Asympt. shedding
3. Sympt. unrecognized

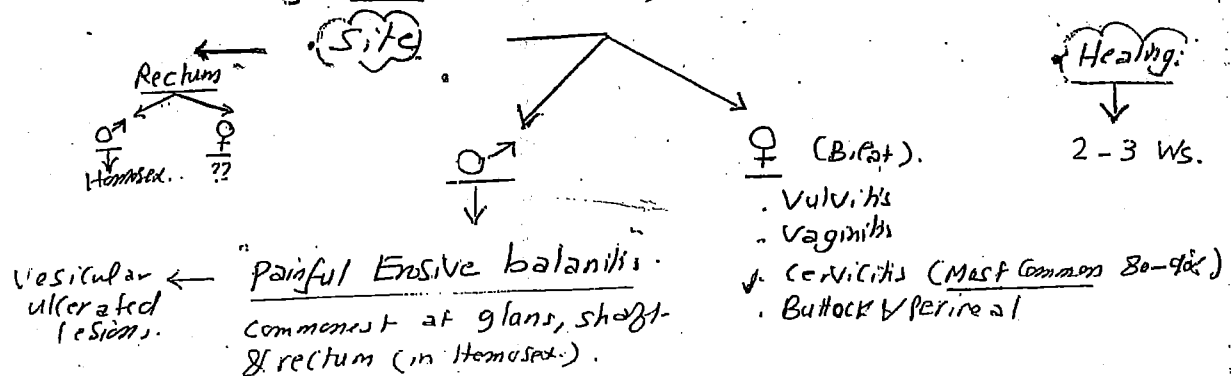
CIP

(A) primary inf. (< 90% Asympt.
10% Sympt)

1. IP: 2d - 2 wks (usually 3-7 ds)

2. Prodrome (local systemic)

3. Lesion (No grouping of vesicles).



B. Recurrent inf.: (Reactivation):

1. Recurrent cause, incid, No., types

2. Problems — local (+) (Mild)
Syst. (-)

3. Lesions Col & grouping of vesicles

Site: → same Region but not
The exact area (generally below
Waist).

Healing: 1-2 wks.

(H. labialis — 1, 2)

NB 1. Recurrent inf. usually (>50%) Asympt.
or Sympt. unrecognized.

2. Initial non 1ry inf. is more mild >
The primary inf. (s.d.) Neutralising Ab.
"Cross Reactivity"

Complications of H. Genitalis:

• More Common in:

H.A.E.M.

1. Women 2. 1ry inf.

• include:

1. 2ry bact. inf. (Most Common) ± Scarring

2. Extragenital lesions (20%, cut. or Syst.)

3. Urine Retention (15%): d.t.

• Lumbosacral radiculopathy

• Reflex pain inhibition d.t.

intraurethral lesions.

4. Aseptic Meningitis. (Fever, Headache,
Vomiting & photophobia)

5. Neonatal H.S.

← 6. Cancer Cervix.

7. Depression / Psychosexual problems.

8. H.A.E.M

9. Eczema Itentia

So
Recurrent HS
of Cervix
→ do
Cytological
Smear / Y.

Mode of Transmission:

1. Antepartum (Transplacental): (5%)
2. Intrapartum: during delivery (85%)
3. Postpartum: non maternal source (Kissing by infected adult) (10-15%)

(So there are 2 Sources: Maternal & Non-Maternal).

Risk of Inf.

- A. Episode: 1st Episode attack of mother is more dangerous > recurrent Episodes in causing Neonatal Inf. Why?? (in recurrent Episodes the fetus is protected by Maternal IgG)
- Incidence to the episode.

(1) True 1st Episode → 50%

(non 1st episode) → (2) initial non 1st episode → 30%

sep ↓

(3) Recurrent episodes & asympt. shedding → 0-4%

B. HSV₁ > HSV₂ (despite its less common).

C. presence of active lesions at time of delivery.

D. PROM

X E. Using Fetal Scalp Electrode.

NB: • The most serious is women w 1st Inf. & having active lesion caused by HSV₁ at time of delivery. However most cases are d.t Asympt. shedding.

CIP

22-1

Antepartum (Transplacental)

- Abortion
- IUFD
- Prematurity
- Cong. Anomalies: ^{not}
 - Microcephaly
 - Microphthalmia
 - limb hypoplasia
 - Encephalitis

- Skin effect: extensive Cong
Vesicles & Erosions → Healing &
reticulate scarring & usually Fetal

Intrapartum (Commonest)

3 Types of affect

1. SEM: localized inf
of skin, Eye & mouth.
2. Localized CNS affect.
3. Disseminated inf.
(Multiple organs) ^{CNS} Lung Renal
4. Non specific Symptoms
as: irritability, poor feeding
& lethargy.

Complications

- Seizures
- Psychomotor retardation
- Spasticity
- Blindness
- Learning disabilities
- Death.

- NB: Transplacental Transmission: has poor prognosis &
High Morbidity & Mortality
- Intrapartum Transmission: has better prognosis
& > 90% develops normally.

DNNZ

Eczema Herpeticum

(Kaposi Varicelliform Eruption)

HSV ing (1 or 2) + any of the following condition:

usually first episode

- [AD
- [SD
- [scabies
- [Ichthyosis
- [Darrier
- [Hailey-Hailey
- [pemphigus
- [pemphigoid

spread of HSV throughout the diseased areas (Eczematous Areas)

(at CMI or Impaired barrier)

CIP (DNNZ)

① IP: 5-12 d after exposure to individual with 1st episode of HSV mf. (either sympt. or asympt.)

② FAHM

③ Clusters of itchy &/or painful blisters start usually at head & neck on active or healed site of previous skin dis. (e.g., AD) 7-10 d → New patches appear at other diseased areas w may become Generalized 2-6 w ± Healing is small white scars.

Fever
Severe pain
Vesicles
Punched out Erosions

CLUE for Diagnosis

The lesion char: monomorphic, umbilicated
Vesicles filled with clear, cloudy or Hgic fluid → Hgic crust formation → painful punched out bleeding Erosions.

④ 2nd bact. inf. may occur

⑤ In severe cases → systemic organ affected e.g. Eyes, CNS, Lung, Liver → fatal

NB: other viruses may cause Eczema Herpeticum

Small pox → Vaccinia virus → Eczema vaccinatum
Hand-foot-mouth dx → Coxsackievirus A16 → Coxsackium

NB when caused by HSV it's called Ecz. Herpeticum but when the causative virus is unknown it's called:

Kaposi Varicelliform Erupt^{on}

Treatment: (1) ACV or VCV: oral or IV

(2) Antibiotics

(3) Consult ophthalmologist if Eye affected

Ocular H.S (Herpetic Keratoconjunctivitis)

Specificity

Trifluoridine

(Virostatic) antiviral

Keratitis, Conjunctivitis, Corneal ulcer & ± Ectopic effect

• Preauricular L.N

• 2nd commonest cause of Corneal blindness in USA

• w/it HSV₁ or HSV₂:

• if neonatal → usually HSV₂

• if older than neonate → " HSV₁

Herpetic whitlow

digital H.S infection occur in:

• children: e. oral H.S

• dentists & medical personnel

• digital/genital contact

HSV₁

→ HSV₂

Herpes Gladiatorum

H.S infection occurs among wrestlers or during practice of sports at close contact.

Herpetic syphilis

H.S Inf. of beard & moustache of Adult → Viral Folliculitis

Herpes infection in special situations

[A] In immunocompromised:

1. Chr. ulcerative H.S: persistent erosions & ulcers in Face & perianal area.

2. Acute Generalized: (Varicella like):

wide spread varicellar eruption (as Varicella) → death

3. disseminated visceral

4. More frequent shedding

5. ACV Resistant H.S

use FosCarnet Cidofovir

[B] HSV + HIV

more severe outbreaks
More frequent viral shedding

use Anti HIV + ACV (if No Resistance)

Verrucous
Exophytic
Pustular
ulcerative

lesion +

use Anti HIV

Q. How to differentiate bet. 1st & Recurrent attacks.

(See Q20 - Labial H.)

Q. Whole duration of dis outbreaks??

- Primary attack : 3 wks.
- Recurrent " : 1 w.

Q. Does Frequency of Recurrence will ↓ over the time?? ^(without H)

- over longer periods (3-5 Ys) Frequency of outbreaks will ↓.



Q. Why genital Herpes is a problematic disease??

Friend of life

because it is not curable so associated to social stigma:

- Emotional stress
- Anger
- Depression
- Guilt

So psychological aspect should be evaluated well.

Diagnosis of H-V

(Type of)

1. Tzanck smear: bed side test

Rapid preliminary procedure that can be used in office.

Non-specific (Can't diff. bet. HSV1 & HSV2 or even VZV)

Results → 60-90% accurate
→ 3-13% false pos.

Method: Recently developed vesicle (48 hrs) → de-roofed

→ Absorbant Gauze for Fluid → Swabbing the

base then examined by Mic or stained then examined

→ Multinucleated giant cells. (Toluidine)

tel serum obtained (A/Bleeding) directly

2. DFA ^{Rapid} sensitive ^[السرعة والسهولة] diff. bet HSV1 & HSV2

3. Culture: differentiate bet. different types & can be available within 2-5 days. (on HeLa Cells)

4. PCR: good as culture: used to detect DNA of the virus in CSF

2nd General ELISA

Western Blot

5. Serology:

1. detect asympt. carriers.

2. determine inf. rate in various populat.

3. detect complex at risk for neonatal H-S

Very good for detect of Glycoproteins: gG1 → HSV1, gG2 → HSV2

WB is FDA for det & prev. eng.

6. Histopathology

→ ① Ballooning degen of KCs with intra-nuclear Inclusion Bodies (degeneratⁿ & Marginatⁿ of chromatin)
→ Blistering (at level of st. Spinosum)

② Multinucleated Giant Epidermal Cells:

Formed by fusion of infected (KC)
nuclei are fit or molded together as pieces of puzzle. (Clas)

NB: Depends on lesional Morphology!

- Acute Vesicular lesion → do track.
- Crusted, eroded or ulcerative lesion → others

Complications of H.S.V. 1 & 2 types

- ① 2nd bact. Inf.
- ② Corneal ulcer, opacity
- ③ dissemination → Hepatitis, encephalitis & Pneumonia.

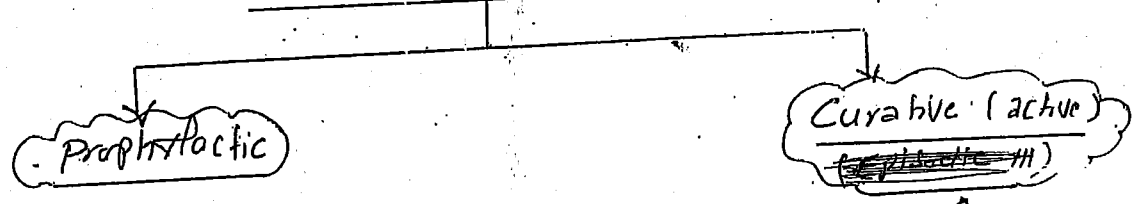
4. HAEM (Hargen ass. Erythema Multiform):

H.S is the commonest cause of Recurrent EM
usually after: ① daps.

(E) pts →

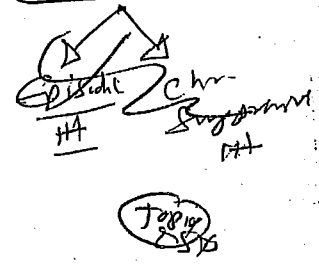
5. Neonatal H.S
6. Eczema Herpeticum
7. Cancer Cervix.
8. Complications of genital

Treatment of HSV inf



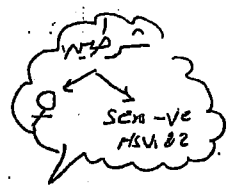
A. For Herpes labialis (HSV1),

- ① Avoid triggers e.g. UVB give sunscreen.
- ② prophylactic Antivirals before
 - 2-4 hrs before or at morning of the procedure & for 2 wks after that (FCV: 250 x 2 / VCV: 500 x 2)



B. For Herpes Genitalis (HSV2),

- ① Avoid sex: (the only sure protective method).
- ② Condom use: prevent transmission from ♂ to ♀
- ③ Vaccine: Glycoprotein D HSV2 Vaccine.
 - for prevention of HSV2 in women
 - That's Sero-ve for HSV1 & HSV2
 - [Also: lipidone G & H vaccines]



C. For prevention of Neonatal HSV:

- ① Cesarean Sect: For all cases & active lesions or prodromal symptoms or PH & HSV inf.
 - Transplacental infection
 - doesn't prevent inf. Completely??
 - Expensive.
 - ↑ Morbidity.
- ② Recently: Measures taken if
 - The ♀ & ♂ are Sero-ve
 - The ♀ Sero-ve & ♂ Sero-ve
 - ♀ is Hx of recurrent HSV1.

Measures For:Wife:

- Avoid Sex in 1st last trimester
- Vaccine (see above)

Husband:

- Condom
- ACV: suppressive H.
- (during last trimester)

✓ 1/3-1/4 in Last Trimester (at 36 w) ↓ incidence of vaginal & Transplacental.

D. Prophylactic chr. suppressive therapy

for recurrent inf. (HSV1 & HSV2):

Indications:

1. recurrent inf. > 6 outbreaks / Y.
2. recurrent HAEM > 1 Y.
3. physically or emotionally severe outbreaks.
4. Insufficient prodrome to benefit from Episodic H. (لوحظ الفتره دي لحد ما حطت الحبوب)
5. Immunosuppression (post transplant)
6. suppressive H. for sero-ve couples.

7- post herpetic vitilligo.

• Dose, → see H. of H. Genitalia.

(دوسيا). NB: → Resiquimod 0.01% gel is used
 • Topically applied Immune response
 Modifier used to ↓↓ recurrence.

Active (episodic/curative) treatment of HSV infection

Topical

① ACV 5% Creams:
 دواء كل ٤ ساعات ٥ مرات في اليوم
 على HSV

② Penciclovir 1% Cream:
 دواء كل ٤ ساعات ٥ مرات في اليوم
 على HSV

③ Docosanol 10% Creams:
 دواء ٥ مرات في اليوم ١٠٪ في ١٠ أيام

④ ACV + Topical Cs
 Hydrocortisone 2%
 or
 fluocinonide 0.05%

Systemic

- ACV
- VCV
- FCV

↓
 الجدول

FDA approved for
 Herpes Labialis

Type of Inf.	Treatment
"Recurrent H. labialis" أعراض متكررة في الشفاه (problematic)	<ul style="list-style-type: none"> • ACV: (400) → ٥ مرات في اليوم ٤ ساعات • VCV: جرعات مرتبة يوميا ٤ ساعات • FCV: ١٥٠ جرعات جرعة واحدة
✓ H. Genitalis	1st attack - Recurrent -
✓ Neonatal HSV inf.	ACV: (IV) 10mg/kg every 8 hrs For 10-21 days
✓ Immuno Compromised	ACV oral: 400 X 5/d or IV: 5mg/kg / 8hr VCV FCV (duration) until all lesions healed

Not FDA approved.

→
 جرعة واحدة

→
 الجرعة الواحدة

<p>• <u>ACV resistant HSV</u> Inf. in Immuno-Compromised + HIV</p>	<p>• <u>Foscarnet</u> (IV) 40 mg/Kg every 8-12 hr for 2-3 wks (or until healing) [FDA approved] → not preferred (nephrotoxic)</p> <p>• <u>Cidofovir</u> 1% (Cream) → لا يُفضل (No SE) علاج 3-5 أيام على المنطقة المصابة [CDC approved]</p>
<p>• <u>Chr. suppression</u></p> <p>↓</p> <p>in setting of NL individual in setting of HIV inf.</p>	<p>→ See Genital H-H & EOLingia.</p>

• General Considerations

A. Guidelines For Antivirals in H of HSV

① should be given during the 1st 48 hrs or during the prodrome (tingling, numbness, burning) to be effective.

② Its value is: ↓ Pain, ↓ shedding, ↓ Healing time.

③ Chr. suppressive H value is:

↓ Asymptomatic shedding by ~95%

↓ recurrence by ~80-90%

B. Topical ACV Cream: FDA approved For limited

Mucocut inf. in ImmunoCompromised while its

use in ImmunoCompetent may be not effective & may cause resistance to systemic ACV

→ نادرًا ما يكون فعالاً

لا يُفضل استخدامه في المرضى الذين يعانون من ضعف المناعة

C. peniclovir 1% & Docosanol → FDA approved For recurrent H. labialis

D. Systemic ACV: not FDA approved For H. labialis but used by authors / FV/VCV → approved.

A. 1st attack → 10 days (7-10).

Tab:

ACV (400 mg)

VCV (500)

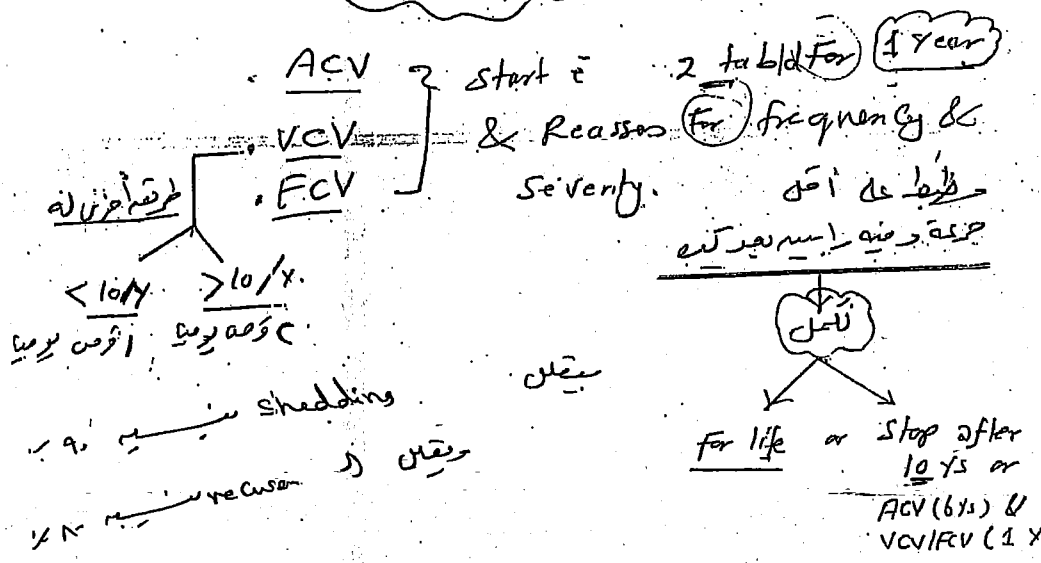
FCV (250)

ACV (3) 3-5 times a day or 200 mg 5
VCV (4) 4 times a day
FCV (3) 3 times a day

B. Recurrent attack For 5 d (5-7 d).

ACV → 3 (daily)
VCV → 2 tab/d
FCV → 1 tab/d

C. Chr. suppressive therapy (> 6 Recurrences/Year)



Warts (Verrucae)

Benign ^{epid.} proliferation (Tms) caused by Human papilloma virus (HPV) Inf. of skin & MM.

HPV belongs to Papovirus group & are:

- slowly growing
- double stranded & naked
- (no envelope: so resist drying)
- > 100 types of HPVs discovered.

Mode of Transmission:

1. Contact
 - Direct: e.g. ^{Hand to hand} ^{المصافحة}
 - Indirect: e.g. ^{shared towel} ^{مناشف مشتركة}
 - Autoinoculation: (causes local spread.) e.g. ^{itching} ^{حكة} "Pseudo-kobner"

2. Sexually transmitted

3. Vertical: Perinatal during vaginal delivery. Laryngeal papillomatosis

Types of infection:

1. Clinical: Lesions seen by Gross inspection.
2. Subclinical: lesions seen only by aided exam. (acetic acid soaking). ^{revised}

3. Latent: presence of HPV virus or viral genome in apparently N.L. skin.

Thought to be common specially in Genital warts & explains in part the failure of destructive methods to eradicate warts.

Why Recurrence is common

HPV Classification

According to Type of infection.

(See below)

According to Risk of Malignant Transformation

- Non Risky group**
 - 4 types: 1, 2, 3, 4
- Low Risk group**
 - 6, 11 types
- High Risk group**
 - usually: < 16, 18, 31, 33, 45
 - Also:
 - HPV 6 (+)
 - HPV 5 & 8

دواء كولي كول
 6 & 11 : Low risk
 16, 18, 31, 33, 45 : High Risk

HPV Infection: "Ag"

Genital

Non genital

High Risk HPV (16, 18)

Low Risk HPV (6, 11)

Cutaneous

Mucosal

- * Bowen's dis
- * Bowenoid Papulosis
- * High grade intraepithelial Neoplasia.
- * Giant Condylomata Accuminata of Buschke-Lowenstein

- * Condylomata Acuminata
- * Low grade intraepithelial Neoplasia. (CIN)
- * استثناء انفا سيكا (HPV 6)

- * Cut. warts.
- * EDV

1. Laryngeal
 - Papilloma
 - Cancer
2. Conjunctival
 - Cancer
3. Oral
 - Papilloma
 - Cancer
 - Leukoplakia
 - Heck's dis.

NB كل نوع من الفيروس ينتج نتائج مختلفة.
 يمكن ان ينجح العلاج بعد عدوى ذات كائن مختلف.

Common ↔ Genital

لرئوي DD +
 Cowden's dis
 +
 Cancer (thyroid, Breast, trichilemmoma, oral papilla)
 (cobble stone)

"HPV of Genitalia"
classified into

(8)

P. 57

• Low Risk or Benign types.

≈ 12 types of HPV

• Commonest: 6 & 11

① Condylomata Acuminata
(Condyloma Acuminatum)

② low grade IN

• High Risk or oncogenic types

• ≈ 15 types of HPV.

• Commonest: 16 & 18
(also 31, 33)

① Benign Papules

② Bowen's dpl.

③ Buschke-Lowenstein Tm.

HPV 6

④ Intraepithelial Neoplasia

High grade

• Vulvar IN (VIN)

• Cervical IN (CIN)

Condylomata Acuminata (Genital wart).

• Most Common STD among sexually active young adults in USA & Europe.

• Most infections are Latent or subclinical & this is responsible for high incidence & recurrence following H.

• Genital HPV inf. of great importance in women than men d.t. Risk of Cancer Cervix.

• Genital HPV inf. closely linked to Cancer:

← Cervix
glans
anus
Vulvovaginal area.
Perianal area.*

• Natural Hx of Genital warts:

• Most cases → lasting (1-2 yr) then resolve.

• Few cases → persist.

• fewer " → Cancer.

Other factors that ↑↑ Risk of Malignancy of HPV:

(9)

- ① Location of infection
- ② Smoking
- ③ Uncircumcision (in ♂)
- ④ Immuno suppression
- ⑤ Sex
 - early: before 17 yrs age (Highest Risk)
 - Multiple: 6 or more
 - Prostitution

follow up
& pap
smear.

Transition Zone
of Cervix
Anus

HPV Types: 30 types may be responsible for Genital warts
& more than one type usually exist in one patient.

Type: HPV: 6 & 11 be.
(Bg or Low risk to Transformed to Mg).

Site: may affect:

- ♂ → penis
- scrotum
- anus
- intraurethral (hematuria or Altered stream)
- ♀ → vulva
- cervix
- anus
- perineum
- intraurethral.

Clin: 2 clinical Varieties: according to the site:

on dry surfaces

- Penis
- Scrotum

Hyperkeratotic Common -
wart like papules

on moist exposed surfaces (Perianal & Perineum)

Cauliflower mass

- pedunculated
- Flesh Colored
- Verrucous
- Bleeds easily

no size →
Polocephalin.

Genital warts in children

Transmission may occur d.t:

- ① Vertical transmission perinatally. (انتقال الولادة)
- ② digital autoinoculation (الخطبة)
- ③ fomites
- ④ social non sexual contact
- ⑤ Sexual Abuse. / ٤ - ٦ - ٧ - ٨ - ٩ - ١٠ - ١١ - ١٢ - ١٣ - ١٤ - ١٥ - ١٦ - ١٧ - ١٨ - ١٩ - ٢٠ - ٢١ - ٢٢ - ٢٣ - ٢٤ - ٢٥ - ٢٦ - ٢٧ - ٢٨ - ٢٩ - ٣٠ - ٣١ - ٣٢ - ٣٣ - ٣٤ - ٣٥ - ٣٦ - ٣٧ - ٣٨ - ٣٩ - ٤٠ - ٤١ - ٤٢ - ٤٣ - ٤٤ - ٤٥ - ٤٦ - ٤٧ - ٤٨ - ٤٩ - ٥٠ - ٥١ - ٥٢ - ٥٣ - ٥٤ - ٥٥ - ٥٦ - ٥٧ - ٥٨ - ٥٩ - ٦٠ - ٦١ - ٦٢ - ٦٣ - ٦٤ - ٦٥ - ٦٦ - ٦٧ - ٦٨ - ٦٩ - ٧٠ - ٧١ - ٧٢ - ٧٣ - ٧٤ - ٧٥ - ٧٦ - ٧٧ - ٧٨ - ٧٩ - ٨٠ - ٨١ - ٨٢ - ٨٣ - ٨٤ - ٨٥ - ٨٦ - ٨٧ - ٨٨ - ٨٩ - ٩٠ - ٩١ - ٩٢ - ٩٣ - ٩٤ - ٩٥ - ٩٦ - ٩٧ - ٩٨ - ٩٩ - ١٠٠ - ١٠١ - ١٠٢ - ١٠٣ - ١٠٤ - ١٠٥ - ١٠٦ - ١٠٧ - ١٠٨ - ١٠٩ - ١١٠ - ١١١ - ١١٢ - ١١٣ - ١١٤ - ١١٥ - ١١٦ - ١١٧ - ١١٨ - ١١٩ - ١٢٠ - ١٢١ - ١٢٢ - ١٢٣ - ١٢٤ - ١٢٥ - ١٢٦ - ١٢٧ - ١٢٨ - ١٢٩ - ١٣٠ - ١٣١ - ١٣٢ - ١٣٣ - ١٣٤ - ١٣٥ - ١٣٦ - ١٣٧ - ١٣٨ - ١٣٩ - ١٤٠ - ١٤١ - ١٤٢ - ١٤٣ - ١٤٤ - ١٤٥ - ١٤٦ - ١٤٧ - ١٤٨ - ١٤٩ - ١٥٠ - ١٥١ - ١٥٢ - ١٥٣ - ١٥٤ - ١٥٥ - ١٥٦ - ١٥٧ - ١٥٨ - ١٥٩ - ١٦٠ - ١٦١ - ١٦٢ - ١٦٣ - ١٦٤ - ١٦٥ - ١٦٦ - ١٦٧ - ١٦٨ - ١٦٩ - ١٧٠ - ١٧١ - ١٧٢ - ١٧٣ - ١٧٤ - ١٧٥ - ١٧٦ - ١٧٧ - ١٧٨ - ١٧٩ - ١٨٠ - ١٨١ - ١٨٢ - ١٨٣ - ١٨٤ - 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Transmission acc. to age:

- in 1st year $\xrightarrow{\text{VLE}}$ Vertically
- Age > 3 yrs $\xrightarrow{\text{VLE}}$ Sexual Abuse.

• Spont. Resolution often in (75%) of cases. ✓

NB annual pap. smear should be taken from:

- ① female \bar{e} genital wart
- ② Homosexual Male \bar{e} Peri-anal Wart
- ③ any genital wart in Immuno-suppressed

Bowenoid Papulosis

(For details see ^{skin} Cancer)

- HPV: 16 & 18
- Site: may be Genital: Penis, Vulva & perianat.
extragenital: Face & Neck
- Clinically: Flat, sessile, Hyperpigmented papules that difficult to be differentiated from Condyloma Acc.

• path: Abnormal epithelial maturation & cellular atypia closely Resembling Bowen's dis.

• progression to Invasive SCC more on lesions of Penis, Cervix, Vagina, Rectum.

• Females with Bowenoid with their husbands have Bowenoid → Risk of Cervical Dysplasia

Giant Condyloma Accuminatum & Buschke & Lowenstein

• there is a type of SCC called Verrucous Carcinoma or can occur in 4 sites: (all may be caused by HPV)

- AC (Keratin Tm) →
- ① oral cavity → Oral Florid Papillomatosis
 - ② Genitalia → Buschke & Lowenstein Giant Cond.
 - ③ Planter aspect of foot (Sole) → Epithelioma Coriaccatum.
 - ④ Gottron Tm: skin
- Verrucous Carcinoma ch' by well differentiated, slowly growing, Locally MG (rarely metastasize).

Giant Condyloma ACC. & Buschke & Lowenstein:

• Bel. keratosis
• Giant genital wart
• rare aggressive wart like growth (Eccentric condyl. like)
• Caused by HPV 6 (16, 18 w/c Carcinoma & L. cells)

• Site Common: glans & prepuce (if uncircumcised)
Lesser: perianat & Vulvar.

• DD of psoriasis les
• Basic cell C-sep
• Bowenoid
• Extramammary p-ges
• Multiple plane wart
• Keratin is verruciform
• Epidermal dysplasia verruciform

(15) D.D of Genital warts = Causers of Papular / nodular Genital lesions

DD of condyloma acuminata

Sexually transmitted diseases

- 3 | • Condyloma latum (syphilis): broad-based, smooth-surfaced lesion.
 • Herpes simplex virus (HSV): vesicular eruption with red base and ulceration.
 • Molluscum contagiosum: umbilicated yellowish papules with central core.

Common benign skin lesions

- 3 | • Nevil: typically raised, but pedunculated types may occur.
 • Ectopic sebaceous glands (Fordyce spots): small, yellow papules on genital and oral mucosa.
 • Pearly penile papules: circumscribed papules, 1-2 mm in diameter, usually over the proximal edge of the glans penis (considered normal anatomy).

Neoplasms (biopsy required if suspected)

- 3 | • Bowenoid papulosis: ~~multiple~~ single or multiple rough papules, 2-4 mm in diameter, flesh-colored to red-brown, recalcitrant to usual wart therapies.
 • Malignant melanoma: typically single, may be flat or raised with variable color and shape.
 • Giant condyloma of Buschke-Löwenstein tumor: low grade, locally invasive malignancy that can appear as a fungating condyloma.

→ pigmented
 → flat
 → sessile

do Biopsy if there is
 Controversy."

Cond. Acuminata	Cond. Lata
• HPV	• T. pallidum
• Cauliflower	• Flat
• Flesh colored	• Greyish
• Verrucous Surf.	• Smooth Surf.
• Pedunculated (its)	• Sessile
• bleed easily	• don't bleed easily

NB: Malignant transformation in non-genital wart is rare
 But may occur & so called: verruca carcinoma that
 may occur on any area but commonest is planter
 surface (epitheloma conicatum).

→ A typical, non resolving wart on ^{hand} penungual unit should be
 Biopsied to rule out SCC as can mimic wart specially
 in the Region of nail unit.

Treatment of Condylomata.

(22)

Goal of Ht: Removal of exophytic lesions & Amelioration of symptoms.

No Ht has been shown to eradicate HPV completely
d.t. common Latent & subclinical infection. (50)
it may be considered Friend of Life (as H-S.V2)

Treatment

Prophylactic

- ① Avoid sex
- ② Safe sex
- ③ Condom
- ④ Vaccines

Gardasil
(HPV4)

[against HPV 6, 11, 16, 18] (E)

For ♂ & ♀ at 9-26 y.

Cervarix
(HPV2)

[against HPV 16, 18]

For ♀ at age 10-25 y.

Dose: 1 day, 2ms / 6 ms.

(3)

Efficacy:
↓ Genital wart (62%)
↓ High Grade CIN

Curative

1. Antimitotics

- Podophyline resin
- Podophylo toxin

2. Anti Neoplastic

5FU

Cis

3. Desiccants → TCA

4. Immunoresponse Modifier

- Imiquimod
- IFN α2b

5. Surgical Methods

- Electro
- Cryo
- Endoscopic surgery
- CO2 laser

- ① - Inf about high risk of recur
- ② - No relation ext Ht & recur
- ③ - is only modality antine Ht to 3 months to 5y follow
- ④ Benign neglect
- ⑤ No aggressive Ht
- ⑥ Friends of life

الرطوبة
 Podophyllin Resin 25%
 in Tr. Benzoin (طارة الخشب)

Crude

Extract of dried roots of the May apple plant.

Contain many ingredients: the most active is Podophyllotoxin

Used in Tr. Benz
 Alcohol (10-35%)
 Glycerin

من مرقه شجرة الخشب
 طارة الخشب وكره الخشب
 طارة الخشب

C-I Pregnant (Teratogenic & death) X
area > 10 cm² sys absorption
 ulceration & Bleeding

Less effective in
 dry surfaces: glans, scrotum & labia

Pregnancy [X]

Podophyllotoxin 0.5%
 (طارة الخشب)

Purified extract of Podophyllin resin (the most active ingredient in it)

So don't contain any of the ingredients responsible for toxicity of podophyllin

More effective > Podophyllin

Podophyllin Resin

دواء مرقه شجرة الخشب
 طارة الخشب وكره الخشب

Pregnancy [C]

تحت مراقبة طبية

[3] 5FU

Thymidylate synthetase enz → DNA Synthesis
 → Cellular Prolif. & Viral replication

Limited data about Efficacy in genital wart.

± used for: intraurethral wart.

Pregnancy [D]

[4] TCA: used on Moist warts → Caustic

Trichloroacetic efficacy?

Pregnancy [C].

90% Conc.

دواء مرقه شجرة الخشب (طارة الخشب)

(up 77) 15. Imiquimod \leftarrow (Zyclara)[®] 3.75% & 5%

• Mechanism Immune response Modifier ??

(obj) [1] Act on Toll-like Receptors TLR8 on Monocytes & Macrophages \rightarrow release of:

• IL12
• TNF α
• IFN α

[2] ++ APC

• Preparation

• Aldara: 5% Cream in 250 mg Sack.

• Zyclara: 3.75% & 2.5% C.

• Method: \rightarrow 3-5 times per week for 6 weeks

• Efficacy: More Effective in Mulder warts
Warts on dry areas.

• S.E (1). Irritation: Erythema, Erosion, (excrust), Itching & burning.

(2). Flaking of ps

(3). Hypopigment. (like vitiligo)

(4). Neuropathy

• C.I: Not recommended for \leftarrow intravaginal, vaginal, cervical, rectal & intrarectal Warts.

• Pregnancy [C]

• Children < 12 yrs \rightarrow Safety & efficacy Not known.

[6] IFN-α2b

local inj. is better > systemic.

SE: Fatigue, Fever, Myalgia, Neutropenia, leucopenia, Flu like sympt. (sp, 25)

pregnancy C

children: can be used.

[7] Surgical Methods for large pedunculated polypoid

Electro-, Cryo, CO₂ laser & Endoscopic surgery

↓
of choice for pregnant.

[8] Others → Sinecatechins (Veregen)

مستحضر طبيعي
مستحضر طبيعي
مستحضر طبيعي

(NB) 5FU

1. Flat, hyperpigmented lesion of Bowenoid

2. Intra Urethral wart

P.S.

مستحضر طبيعي

Continuous therapy

twice daily instillation of 5FU in the urethra

↓
irritation

Intermittent therapy

twice weekly instillation of 5FU in the urethra

↓
No irritation

How f choice for

pregnancy → Cryo

Non preg

1. Podofilox

2. Aldara

3. Sinecatechins

For children

Cryo

IFN α2b

Aldara > 12

مستحضر طبيعي
مستحضر طبيعي

Vaccines in STDs

Which STDs have Vaccines?

- Some STDs, such as such as gonorrhea, Chlamydia, and syphilis, are caused by bacteria. They are usually effectively treated with antibiotics, although many patients do not know that they are infective and can spread the disease to other partners. The availability of treatments means that the need for vaccines against these diseases is not a top priority, although the increased resistance of gonorrhea to antibiotics may lead to a shift in priorities.

- Viral STDs are often highly persistent despite current therapeutic options or have no acceptable treatment available. Therefore, vaccines for certain viral STDs are in use, and others are in development.

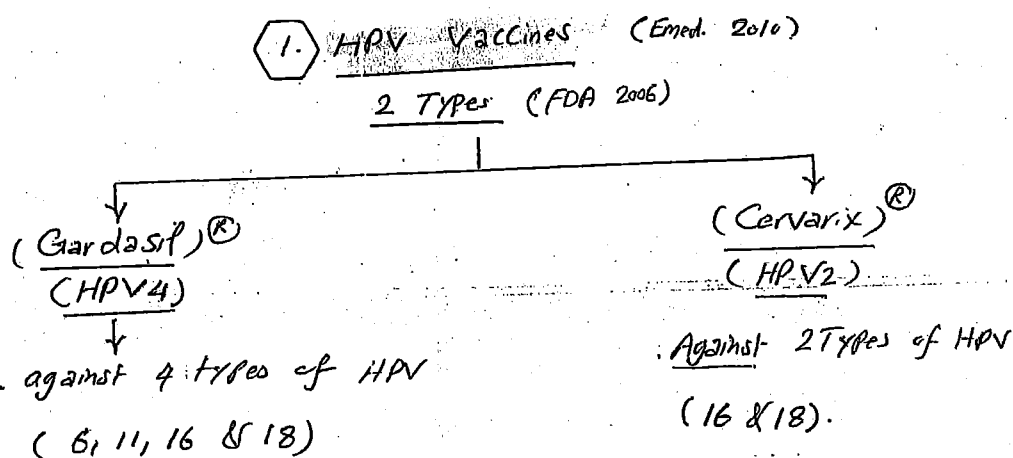
Classification:

A In use vaccines: 1- HPV vaccine

2- HBV vaccine

B In development vaccines: 1- HSV Vaccines

3- HIV vaccine



• Composition: Virus like particles consisting of recombinant L1 proteins from HPV (4 Types in HPV4 & 2 Types in HPV2) [Protein without DNA]

• Administration:

• Gardasil: for ♂ & ♀ 9-26 Ys (recommended Age is 11-12 Ys but can be started as early as 9)

- Cervarix: approved for (♀) 10-25 yrs.

Dose: 3 doses at: 1 day, 2 months & 6 months.

- Efficacy: are more effective before mf. & less effective after mf. (اللقاحات تكون أكثر فعالية قبل الإصابة بالعدوى و أقل فعالية بعد الإصابة بالعدوى)

- in randomised controlled study involving 17622 women Aged 15-26 y →

- ↓ Genital wart by 62%
- ↓ High grade cervical neoplasm by 19% (in vaccinated versus placebo)

Cancer الوقاية من الإصابة بالسرطان
Wart الوقاية من الإصابة بالآفة

2. HBV Vaccines:

Def: recombinant DNA vaccine composed of HBs Ag protein. → Anti-HBs Ag Formant

Dose: 3 doses at: 1 day, 1 m & at 6 ms.

Recommended Populations:

The FDA has licensed several Hepatitis B vaccines for use in the United States. It has been part of the routine childhood immunization schedule since 1994. Following are the general recommendation for use of the vaccine:

Hepatitis B vaccination is recommended for all children, starting at birth in a three-dose series spread over many months. Additionally, all children and adolescents under age 19 who have not been vaccinated are recommended to receive the vaccine, as are adult populations at risk of HBV infection.

B- Indevelopment vaccines

1- Genital herpes vaccines:

- Vaccines for HSV are undergoing trials. Once developed, they may be used to help with prevention or minimize initial infections as well as treatment for existing infections.

Vaccines under trials:

1- One vaccine that was under trial was Herpevac, a vaccine against HSV-2. The National Institutes of Health (NIH) in the United States conducted a phase III trials of Herpevac.[35] In 2010, it was reported that, after 8 years of study in more than 8000 women in the United States and Canada, there was no sign of positive results against the sexually transmitted disease caused by HSV-2.

2- A laboratory at Harvard Medical School has developed dl5-29 (now known as ACAM-529), a replication-defective mutant virus that has proved successful both in preventing HSV-2/HSV-1 infections, and in combating the virus in already infected hosts, in animal models. It has been shown that the replication-defective vaccine induces strong HSV-2-specific antibody and T-cell responses; protects against challenge with a wild-type HSV-2 virus; greatly reduces the severity of recurrent disease; provides cross-protection against HSV-1, and renders the virus unable to revert to a virulent state or to become latent.[37] His vaccine is now being researched and developed by Accambis (acquired by Sanofi Pasteur in September 2008), and is due to be applied as an Investigational New Drug in 2009.[38]

3- A private company called BioVex began Phase I clinical trials for ImmunoVEX, another proposed vaccine, in March 2010

NB. For HSV inf. ✓

Recent: genetically engineered growth defective HSV mutant vaccine was designed to induce Th1 immunity by deleting ICP10PK (The polarizing Gene)

↓
 { ↓ recurrence 37-5%
 ↓ severity 8% }

Types of vaccines:

1. inactivated whole virus vaccines
2. live attenuated
3. DNA preparations
4. genetically engineered mutant HSV vaccines
5. Recombinant viral subunit vaccines

Glycoprotein B/D E the adjuvant MF59

↓
 C60

Glycoprotein D & adjuvant Monophosphat lipid A Immuno-stimulant

↓
 C60

Glycoprotein D Type

effective:

(1) -- inf. in 40% of sero-ve
Women For HSV1 & HSV2

(2) -- symptomatic Acquisition in (70%)

(3) Not effective For Men.

2. HIV vaccine

- Progress toward an HIV vaccine has been slow since the virus was isolated in 1983.
- Only three HIV vaccines have been tested in clinical efficacy trials. *It is difficult to make a vaccine for HIV for several reasons:*

- ① HIV mutates, or changes, much more rapidly than most other viruses. Targeting a vaccine to a rapidly changing virus is challenging task for vaccine researchers.
- ② HIV damages the cells of the immune system. But to be effective, a vaccine must trigger the immune system to fight the disease agent. So, a challenge for HIV vaccine researchers is to develop a vaccine for HIV that must interact with the immune system in a way that is very different from the natural behavior of the virus.

To date, researchers have developed several candidate HIV vaccines, but none has performed well enough in clinical trials to be approved.

in use
in dev
HIV HSV
↓
slow action
mild recovery

Syphilis (8)

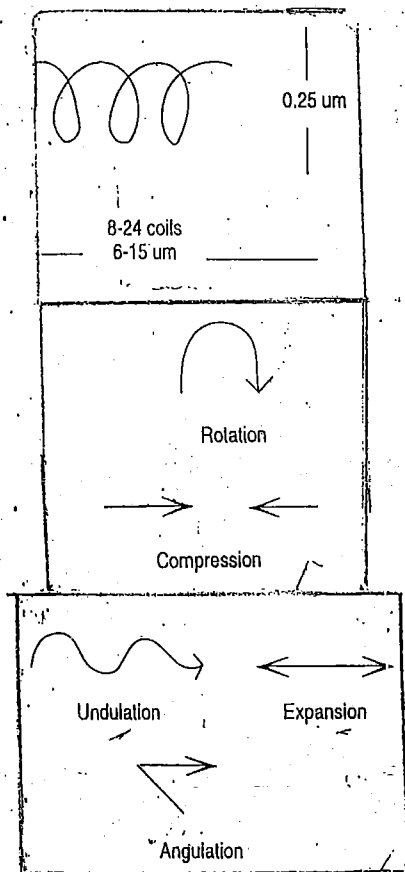
Q pathogen ^{AT} ^{ATC} stages P. 71

• Def → chr. Infectious STD. That can affect Any organ Except Ovaries.

• AET Spirochaete ~ Treponema pallidum Gram -ve

↓
- very weak
- highly infectivity 16-50°

Spiral shaped bacteria with [Biology]



length : 6-12 μm
Width : 0.12-0.24 μm
Coils : 8-24 regular coils.

✓ Movement:

- Locomotion [Corkscrew] →
- Compression
- Expansion
- Angular
- Rotation
- Undulation

✓ Multiplication: Transverse fission.
(1/33 hr)

• Mic Exam:

Conventional
LM

Can't be seen
(level of resolution)
(very thin)

• Stain

Silver → deep brown
Giemsa → faint pink
Immunoperoxidase
IF.

Dark ground (Field)
MIC (DGM)

luminescent against
dark background
+ chit movement

T. pallidum
order: Spirochaetes
Genus: *Treponema*

• Culture: Not Cultured on artificial media
(because they are obligate parasite)

• Can be kept for very short time on TPI medium.

• Non pathogenic T. → Can be Cultured on artificial Media.

✓ • Inoculation: Intratesticular or ID in Rabbits ✓
Heat Hamster

✓ • Viability: destroyed by Drying & Antiseptics.
Soap & water can remove it

• Immunity:

Natural

there is species-variety toward infect

✓ Rabbit is the only primate that can be infected by it.

Acquired. (Extr. - 1.2.3)

HI CMI
Chance Immunity

local
develops 2 wks after appearance of chancre

• if reinfectⁿ occur before development of this immunity

Multiple chancres.

CMI

Seen in 1st stage
(perivascular
infiltr. of
Monocytic
cells)

plasma
cells
lymphocytes

humoral

NB @ Other Spirochaetes:

Pathogenic

• T. Carateum → Pinta

• T. Pertenu → Yaws

• T. Endemicum → bejel

• Borrelia reingens & balanitidis.

Non Pathogenic

• T. Micro & Macro-dentum.

• Rieter strain.

IgM → Predominate in Early stage
IgG → in Late stage: false +ve ear

IgA → 2nd & 3rd stage

These other Treponemes are BY!

• Similar Morphology to T. pallidum.
• Cause different lesions.
• Antigenically different.

Mode of Transmission:

Venereal (95%)
(STD)

Non Venereal (5%)

Direct

- [Kissing
- [biting
- [Breast feeding
- [Transplacental

Indirect

- Contact w/ infected {Towels, cups, secretion}
- Blood Transfusion
- Accidental inoculation (needle)

Pathogenesis (فراشه - ریشه)

(۱-۲-۳)

1st Stage

(chance)

T. pallidum inoculation → local EAO & cellular infiltrate → tissue destruction (chance) → L-N → lesion painless

(EAO: End Arteritis obliterans)

2nd Stage

Blood dissemination, delayed

establishment of Immunity → affects all organs

absent of sympt. signs

Latent

d.t balance bet. Immunity & T. pallidum: (why) ± d.t

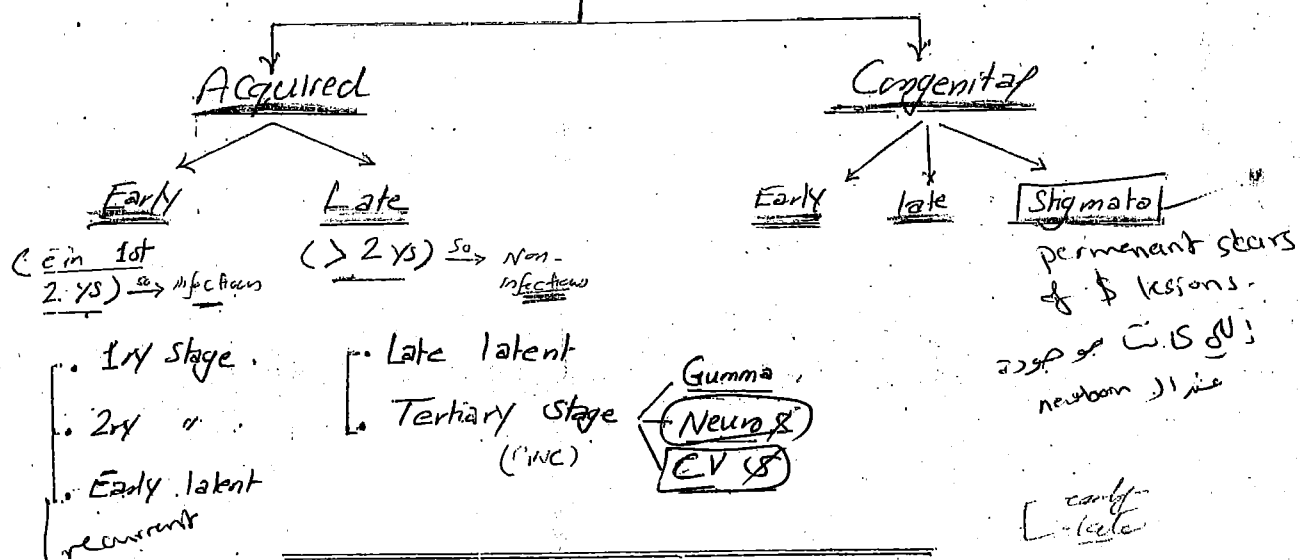
- ① Ass. Immunosuppression (down reg. of Th1)
 - ② T. pallidum ± protected from immune system (sequester intracellular locali.)
- d.t < Coating w/ Host plasma memb.

3rd Stage
(Gumma)

↑ delayed hypersensitivity reaction.
d.t DHR against Relatively Few T. pallidum → Granuloma

Other Mech. : T. pallidum locally
↑↑ in: GPI & Aortic
↓↓ in: Gumma, TD & IK.

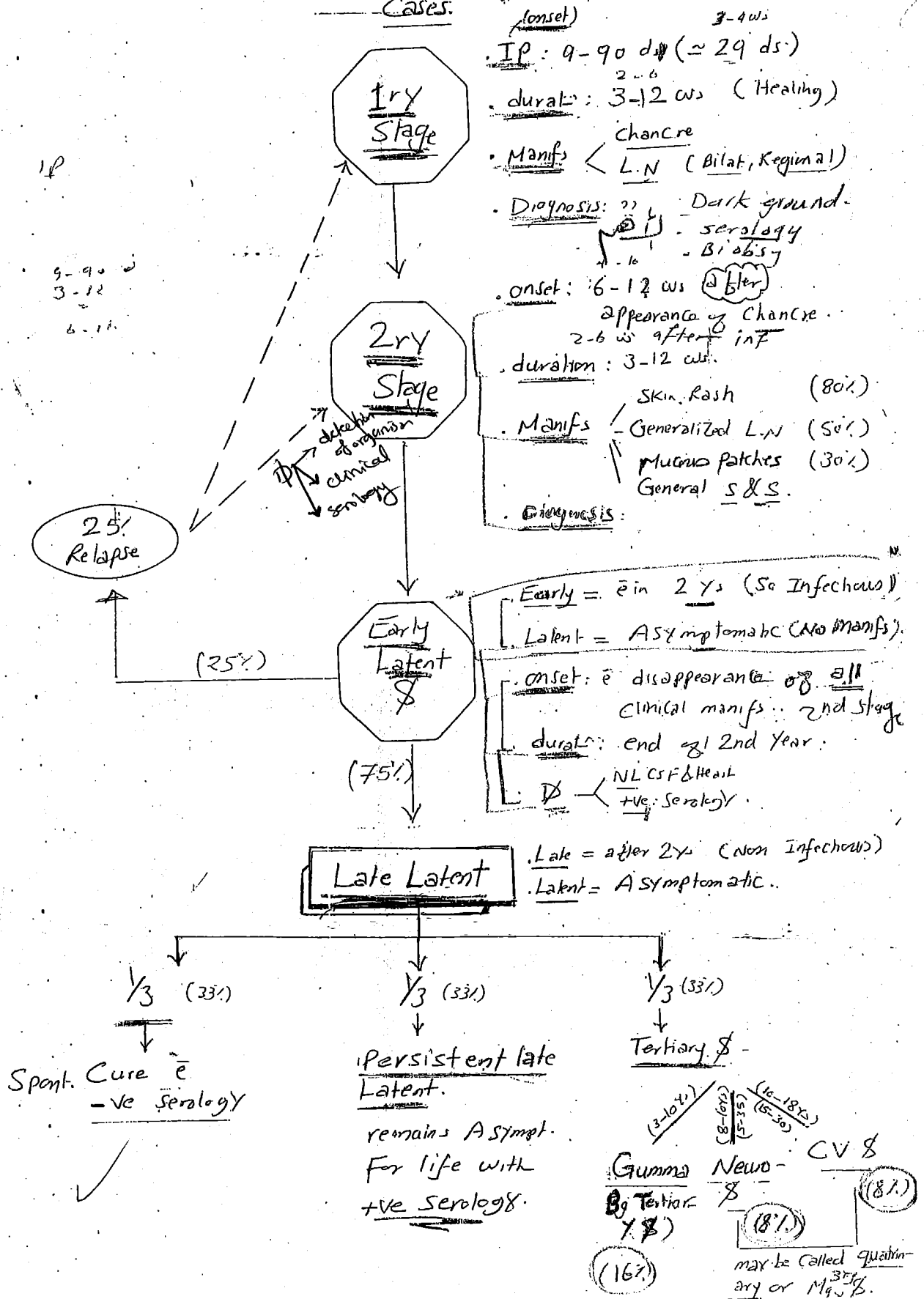
Types of S



Acquired S

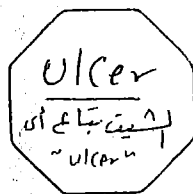
Natural Hx of untreated Cases.

P. 75



1ry Syphilis (chancere)

Chancere starts as Papule → ulcerat



Single
painless
indurated

IP: 9-90 days (usually 2-4 wks, usually 29 ds)

No: usually single (why??); rarely Multiple (absent)

Site: it may be

Genital
(95%)

Extragenital
(5%)

anus
lips
Tongue

Nipple
areola

Succumb



glans
Sutrus
Frenulum
Intra meatal

US (Concealed) → NGU & discharge.



Libae
Urethral &
Cervical (Concealed)

Size: 0.5 - 2 cm

Shape: Rounded or oval.

Edge: ^{Elevated} Sloping Towards Center (Saucer Shaped)

Floor: Clean, pale-red, oozing (serous)

Seen
not felt
Felt Not
Seen

Base: Indurated (like button in tissue).

Tenderness: Painless.

Fixation: → Not fixed.

Single
Painless
indurated

B. 1. → genital

L.N
 (after 1-2w)
 Enlarged
 not tender
 Mobile, rubbery
 Normal overlying skin discrete

arg

Bul

Bi Plat: in genital lesions
 Uni Plat: in Extra genital

Fate: Slow Healing within (3-12w) by

well kept
 Scar

Thin
 Atrophic
 non contractile

NB

Clinical Varieties of Chancre:

HPV

① Absent Chancre: ± d.t.

ملاحظة
 \$ d'emblee
 (seen)

Healed
 Concealed
 Intramural
 Cervix

deep inoculation e.g. Puncture
 Blood Transfusion (also)
 Fullman Balanitis
 Cong. \$

Comp.
 Chancre
 Immunity

② Multiple
 Multiple Infection within 2w
 Kissing: Contagious surfaces: scrotum → thigh
 2ry bact. Inf (Common HIV pts)

③ Painful: if
 Jarisch Herxheimer Reactn
 Combined Yamine

④ Condom chancre → at base of shaft (penile)
 heanoflu

chancre
 (T.P)

⑤ Combined (mixed): Co-infect e H. DUCREY → (Painful)

⑥ Phagedenic: Super Added inf by
 Fusiform bacilli
 Anaerobic
 Spirochaetes
 severe desloughing, Gangrene
 Scarring

effect whole penis → part 3 & high

⑦ Chancre redux: chancre developed on Top of Scar (relapse) of previously Healed Chancre

⑧ Pseudo chancre Redux → Gumma develops on Scar of Healed Chancre

⑨ Edema Indurativum: Chancre + severe Solid edema

⑩ \$ balanitis of fullman: Extensive Circinate or Erosive balanitis
 No chancre

- Absent
- Multiple
- Painful
- Phagedenic
- Condom
- Combined
- Redux
- 9, 10
- Subacute

NB₂ • No L.N (Bubon d'emblée) if:

- congs? (Transplacental) → ① Blood Transfusion • (No $\frac{\text{chancr}}{\text{L-N}} = \text{no 1ry stage at all}$)
- ② Concealed Chancre in Cx → draining to deep iliac L.N.
- ③ Conc. & (No 1ry stage at all).

NB₃ 25% of chancres are Atypical → Multiple, Painful, 2ry bact.

DD: of chancre → Causes of Genital ulcers.

diff. genital

Diagnosis of chancre: 2 Main Inv. / 4 other Inv.

① Dark ground Mic: → "Only sure Method" (or DIF) ↓ For D " [25-92% sensitivity]

the material for examinatⁿ is either from the ulcer or L.Ns. ← no

In order to Remove Scab ✓ / Saprophytic organisms (B. regingesi, B. Balanitides) → Aspirate from L.N

فصل اول
↓ firstly

Clean the ulcer e gauze soaked Saline or water & give

1 gm Sulphonamides / 4 times / d

تحتفظ (to guard @ gainst Sepsis also (has advent. of non Threpanemicidal).

NB (DGM) → Not done for oral lesion d.t Presence of Non pathogenic Treponema (T. Micro dentium Macro " → False +ve (all 12 to 15)

- * indications:
- ① -ve ulcer inv.
 - ② if ulcer is treated by antiseptic applicatⁿ
 - ③ hidden or concealed ulcer.
 - ④ Mouth chancre why??

سؤال

✓ ② Serological Tests: +ve in (50%) of cases (+ve 2w after appearance of chancre)

③ Other Invs

[A] DFA-T. pallidum test: Direct fluorescent antibody

- Done on fixed smear
- Diagnose oral lesions (oral chancre)

[B] PCR

+ [C] Intradermal T.P. Glor test: IV Evans Blue dye. Then Inject Killed "Nichol" strain "ID"
→ Color spot at inoculation site.

[D] Biopsy

→ Indication

↓
In HIV Patients

Why?? because of Abn L

Serological Tests (C) may be $\left\{ \begin{array}{l} \text{very High} \\ \text{low} \\ \text{Fluctuating} \end{array} \right.$

Biopsy → In all & lesions Biopsy
Findings include

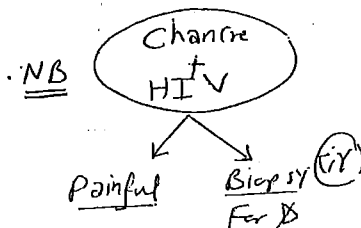
T. pallidum attach to Endothelium → EAO
Heal by scar (obliterated)

في الغالبية العظمى من الحالات
تتكون من

in & → Early
Other dis. → Late

① EAO (at site: Endoth. prolif. → obliterated)

② Plasma Cell-rich mononuclear Infiltrate [per junctional & perivascular infl.]
↳ Lymph. plasma. Macroph.



2ry Syphilis

Not 100%

P. 80

def Stage of Generalization of 1st Blood dissemination; it affects the whole body From: Hair To Toes Except ovaries.

Onset: 6-12 w after appearance of chance
chance: may be healed or going to heal

2-6 w after appearance of inf

(25% of Cases start with presence of chance).

duration: 3-12 w then → "Early latent"

- Manifs:
- ① Skin Rash (80%)
 - ② Generalized L.N (50%)
 - ③ M.M lesions (30%)
 - ④ General Manifs

Gtiathogenesis
↓
Blood disseminat-
of T. pallidum.

(عشيان شتوفه لاسم) Skin Rash (Syphilid) →
Day light (80%)
P-R necessary Pit Rosen

WPL 51
PR
PLEVA
EM DE

General ch

- Generalized, Bilat & Symmetrical
- More common on Flexors
- Flanks & Trunk
- PP (أشعة لاسم)

Poly morphic & Coppery red.

Never

- Itchy → Except (Lichenoid & Condylomata)
- Vesicular
- Scarring: but

Post. Hyperpig.m.
Leucoderma coli: (It's a problem)
residual depigmentat-
surr. by Hyperpig
on the Neck
Specially in
"Brunettes"

- Types
- Macular
 - Papular
 - Maculopapular
 - Pustular
 - Papulosquamous
 - Condylomata lata
 - no vesicles ✓
 - presence of vesicles after

Types of The Rash: (Commonest is Maculopapular):

① Macular (Roseolar) Syphilid:

Macules $\left\{ \begin{array}{l} \text{Rounded} \\ 0.5-1 \text{ cm} \\ \text{Rose pink} \end{array} \right.$

Acne
0.5-1 cm
pustule

② Papular Syphilid: (Commonest)

Papules $\left\{ \begin{array}{l} \text{Rounded} \\ \text{Indurated} \\ 0.5-1 \text{ cm} \\ \text{Dull red} \end{array} \right.$

Variants of Papular Syphilid:

NB
PP lesions
Ch. By

- [Annular
- [Follicular \rightarrow at scalp \rightarrow (Moth eaten) Alopecia
- [Lenticular \rightarrow Lentils like
- [Lichenoid \rightarrow L.p like.

Corymbose: large central papule surrounded by smaller satellite papules

Corona Veneris (Crown of Venus):
(Crown) lines of papules on forehead below 1 ant. hair line.

+ve Ollendorfs Sign:
Papules are Exquisitely Tender to touch of a blunt object.

They are very common & ch. for S

Biett's Collarette: ring of scales surrounding a central papule.

③ Papulo squamous Syphilid:

large scaly papules \rightarrow (Plaque) (Psoriasisiform)

④ Pustular: d.t. ^{Marked} EAO \rightarrow Central Necrosis \rightarrow (pustules)

Black-brown Crusty lesions:

- Ch. By
- ① More in face
 - ② // Immune Compromised
 - ③ // ass. w Neure S

Types

- Small accumulat
- Large
- Flat
- "pustulo-utcerative" (Rupial or Oyster shell syphilitic)

⑤ Condylomata lata = Moist Papules

Most infectious lesion of
(High Ns & T. pallidum)

lesion →

Site: Moist opposed areas & Mucocut junctions

Axilla & groin

Perianal

Genital

Buccal commissures

Condylomata lata	Condylomata Acuminata
<p>→ T. pallidum inf.</p> <p>Flat & sessile</p> <p>Surface $\left\{ \begin{array}{l} \text{Smooth} \\ \text{Moist} \end{array} \right.$</p> <p>Color $\left\{ \begin{array}{l} \text{dull red} \\ \text{Flesh} \\ \text{Greyish-white} \end{array} \right.$</p> <p>Base: Indurated</p> <p>Doesn't Bleed easily</p> <p>→ Moist opposed surfaces</p> <p>→ Inv. $\left\{ \begin{array}{l} \text{DGM +ve} \\ \text{Serology +ve} \end{array} \right.$</p> <p>→ (H) Penicillin</p>	<p>→ HPV inf.</p> <p>Cauliflower & pedunculated</p> <p>Rough (Verrucous)</p> <p>Dry</p> <p>Skin colored.</p> <p>Soft</p> <p>Bleeds Easily.</p> <p>Genital only</p> <p>Both -ve → clinically</p> <p>Podophylline not in pregnant women</p>

Framboesiform Syphilides: Eroded lesions on intertriginous areas
 may proliferate → large, elevated, brown-red
 Crusted patches & dried serum.

NB: DD syphilid form
Drug Eruption:

ix Hx
 rash
 No L.N

any pt
 & generalized
 Dermatitis
 +
 L.N

Consider
2ry S.

أي شيء (2ry S) يشبه
P. Rosacea

② Generalized L.N (50%): As before

Firm, discrete, Non ^{Tender} ~~adherent~~

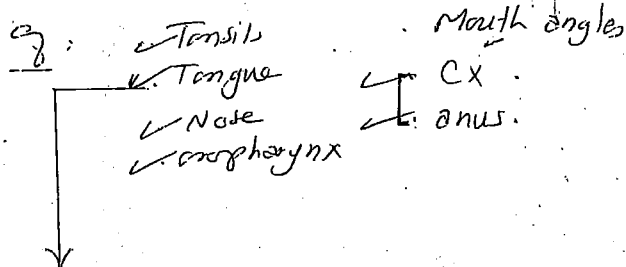
Generalized L.N e.g. cervical, occipital, axillary, epitrochlear.

③ Mucous Patches (30%)

Start as papules or grayish white

Patches → sloughing & ulcerate →

is a "Snail Track Ulcer" or Serpiginous ulcer



dorsal Tongue lesions called: "Plaques fouchées"

in a mucous patches are:

- smooth
- rounded
- dull pink
- destroyed filiform papillae by Necrotic process.

Malignant S
(S Maligna Praecox)

↑
"2w"
Rare Form of S Ch BY:

①. Toxemia & fever ass. e deep ulcerating lesions
That may → death.

Severe

②. oral ulceration & mucous patches.

→ ③. -ve serology ✓

④. More likely to develop Gummas ✓

④ General Manifestations

① Constitutional Manifs : FAHM & anemia

② CNS → meningitis with Cranial Nerve palsies.

③ Eye → Uveitis · chorioretinitis · irregular pupils.
Iridocyclitis · punctate keratitis.

④ Resp. → Hoarseness of voice (d. ulcerates & Edema of vocal cords).
Cough : Bronchial Mucous patches.

⑤ GIT. → Epigastric pain
Nausea
diarrhea.

⑥ Liver → Hepatitis, jaundice & megaly [$\frac{ALT}{AST} \rightarrow$ Similar To HCV
 \uparrow ALP disproportionate
To Transaminase Rise.]

⑦ UT → Nephritis.

⑧ Ms → Myopathy

⑨ Joints → arthritis & Effusion.

⑩ Bones → Nocturnal ostealgia · Periosteitis $\left\{ \begin{array}{l} \text{Skull} \\ \text{Ribs} \\ \text{Sternum} \end{array} \right.$ "Commonest osseous manifs"

⑪ Hair → 2 Alopecia Types \rightarrow "Scalp" & "Tail" loss in §

Diffuse \pm d.t.:

Patchy

① TE (in 3-5ms)

② Jarisch Herxheimer reaction

→ Moth eaten Alopecia at sides & back of Head
✓ Never → Complete

⑫ Nail → Onychia & Paronychia.

Diagnosis of 2ry § (V.P.P.)

① Clinical

② DGM For $\left\{ \begin{array}{l} \text{Mucous Patches} \\ \text{Condyloma lata} \end{array} \right.$

③ Serology (100% +ve) →

Except

Prozone phenomena

Mg & HIV

(So Biopsy)

③ Biopsy

as chronic but less intense
lichenoid. psoriasisiform - granulomatous

Latent S

Early latent S

- 4th
- 1st 2 Ys
 - infectious
 - Asymptomatic
 - +ve Serology
 - 25% Relapse

- onset: after disappearance of 2nd stage
- duration: after 2y
- AIE: \rightarrow at balance
- S/S \rightarrow absent
- D \rightarrow CXR, Echo, Serology

علاج ٢ سنة
وإذا كان سلبياً فليس
إذا كانت إيجابية

Late latent S

- occur after the 2nd year
- non infectious
- Asymptomatic (discovered accidentally during donor or premarital test)
- +ve Serology
- NO Relapse

its danger not d.t infection but the possibility of neurological or Cardiovascular complications

So the following should be done:

* invs for CV S & Neuro S (BY)

① CSF

② CXR & Echo (S/Ambly)

③ "Quantitative" VDRL or RPR

سؤال إحصائي

Relapses In Early S

1/3 of 25% of S patient will relapse within The 1st 2y (Early latent)

Types of Relapse:

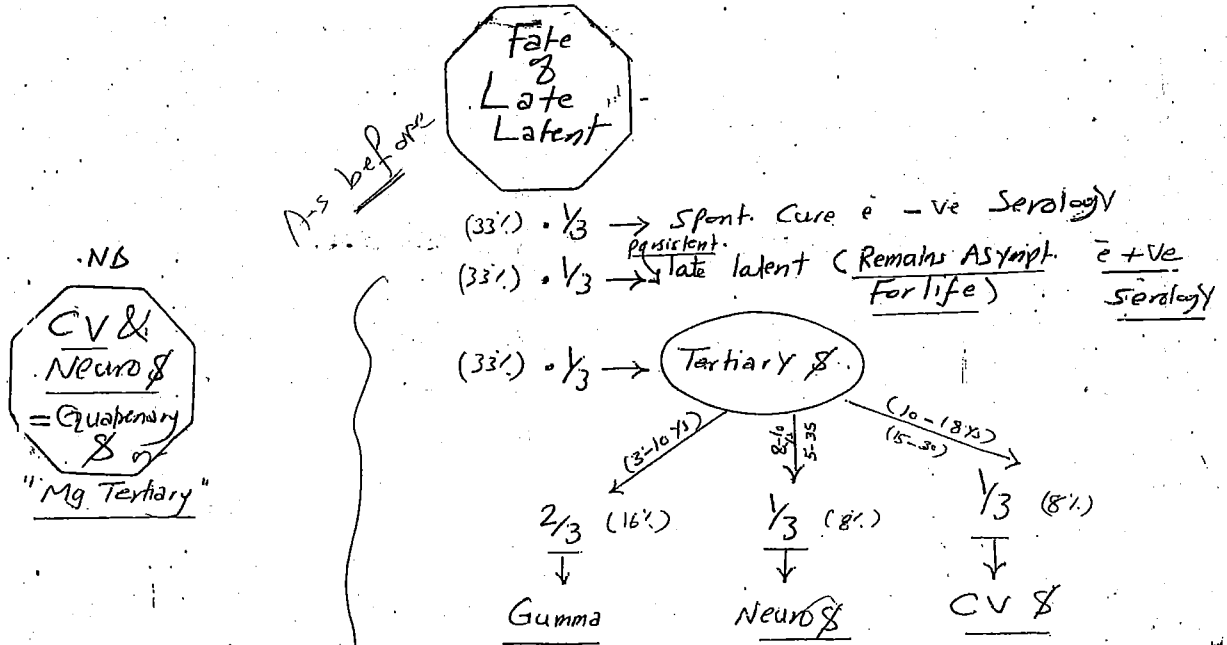
- ① Clinical Relapse: $\frac{1}{2}$ of Recurrence of 2ry S or of Chancre (chancre redux) \rightarrow seen
- ② Serological: change of Reactivity (Sero -ve become Sero +ve or Sero +ve show \uparrow titer; after H)
- ③ Transplacental: apparently cured Mother with \leftarrow Birth of S child Infected by Her Sexual Contact

سؤال: How to differentiate bet: Chancre Redux & re-infection? "See" (Redux show \uparrow titer)

Late (Tertiary) S

P. 86

Def. Late: after 2y. So non infectious • Latent: Asympt.



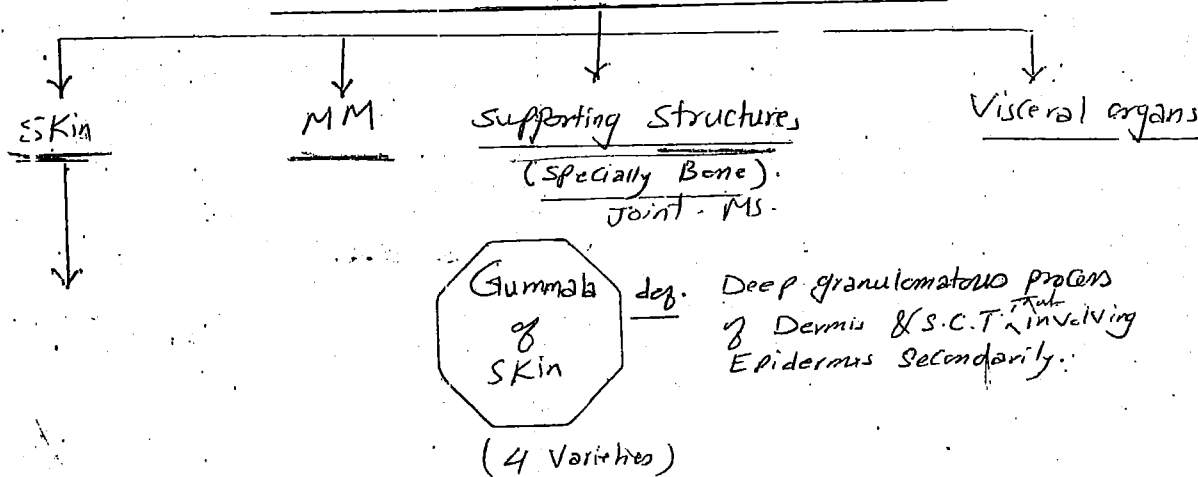
Late S is Ch. Bx → Specific tests: +ve
Non N N: (may be -ve)

Benign Tertiary (Late) of "Syphilis"

P. 87

(Gummata) = Granuloma caused by DTR against relatively low no. of *T. pallidum*.

Any site can be affected. ~~but~~ Commonest is:



① Nodular/Noduloulcerative: • rounded dull red at any site of skin.

painless
Asymptomatic
nodular

• Single or localized in groups i.e. "poly cyclic edges"
✓ Painless
• Fate either $\begin{cases} \text{ulcerate} \rightarrow \text{Punched-out ulcer} \\ \text{Healing} \rightarrow \text{Scar} \rightarrow \text{thin-atrophic (tissue paper)} \\ // \rightarrow \text{Pigmentary} \end{cases}$

② Squamous / Psoriasisiform lesions:

• palmo-plantar large nodules covered i. waxy scaling (similar to ps. but No Auspitz Sign)
• There may be central healing.

③ Subcutaneous lesions: (Most Common):

rounded, painless, S.C. swellings \rightarrow ulceration
Gummatous ulcer \rightarrow (Vertical)

Wash =
thin
leathery

Edge: Punched out i.e. poly cyclic border
Floor: dull red GIT & Wash-leather sloughs
Base: Indurated (Tough yellowish white sloughs)

✓ Pain: Painless.

✓ L-N: No L-N

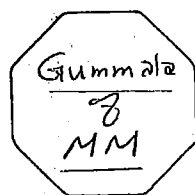
• Fixation: may be fixed to underlying structures

✓ No L-N
✓ Pain
✓ Fixation

Edge : → peripheral Extension → plaques with
PolyCyclic or Arciform border.

Site ^(Trauma Sites) < usually: upper & outer legs (pretibial).
may be: scalp, face, sternum, buttocks.

④ Pseudo-chancere Redux: Gumma appears at site of
previous chancere.



Localized

Diffuse

Painless, Swellings &
Nodules → break down → punched out ulcer

Site: < Nose
Mouth < Vula
Larynx & pharynx
Tongue

↓ painless nodules → ulceration →
Nasal septum & Hard palate → "Saddle
Nose"

① Perforation of

② Destruction of vula → Nasal food
Regurge.

③ Stenosis of < Pharynx → Hoarseness
Larynx → Dysphagia.

Tongue:

may be involved
in all stages of S:

- 1ry → chancere
- 2ry → Mucous
Patches
- 3ry → Gummata

all forms are
preconcerns so
Follow up after H
For Mg.

④ Tongue: affection by Gumma may be:

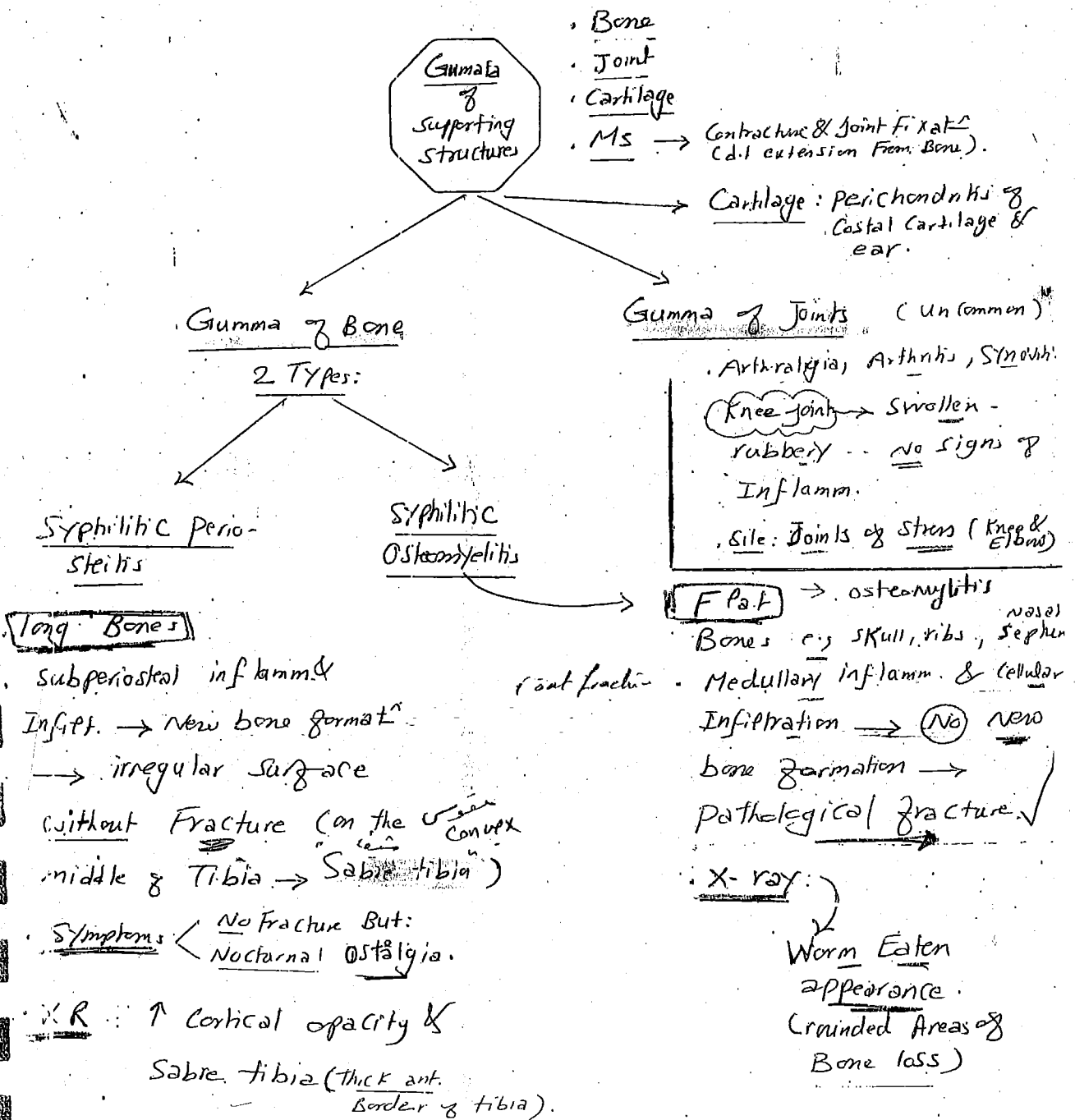
A. Localized → Painless Swellings → punched out ulcers

B. Diffuse → 3 clinical varieties:

(i) scrotal tongue: Deep irregular Fissures
[d.t. interstitial Fibrosis].

(ii) Leukoplakia like: irregular white patches on surface of Tongue → Pre Cancerous

(iii) Chr. Superficial Glossitis: Smooth, red, glazed Tongue: d.t loss of filiform papillae → discomfort & pain.



Wine of Liver

Hepar lobatum

responds to Ht
but therapeutic
paradox may
occur.

Billiard Ball Testis

- Heavy
- painless
- Smooth
- unilat
- ± Hydrocele.

(i / n)

Hepar lobatum

leather Bottle

Stomach

Billiard Ball

Testes

Ant scrotal

ulcerate

PCH

Donath - Lendstein-

er Reacto

Gumma
of
The
Viscera.

(Comment is
liver)

Form of postal
Cirrhosis

liver < Diffuse Gumma : → diffuse interstitial Cirrhosis ()
localized : → Irregular Fibrosis (Hepar lobatum)

Stomach < Diffuse / localized → leather bottle stomach

Respiratory < larynx : → Hoarseness & aphonia
Lung

Testis < localized : oss ē Ant scrotal skin ulcerate
diffuse : diffuse painless
Enlargement ē lost
Sensation (Billiard - Ball testes)

Blood

PCH = Paroxysmal Cold Hemoglobinuria. 2ry to TB epididymitis

Def: Form of Hemolytic anemia that may be rarely associated with late & (Cong. or Acq.)

AET: dt presence of (Hemolysin) combine ē RBCs during Cold Exposure → (Sensitized RBCs)
on rewarming: Sensitized RBCs destructed by Complement

CIP: FAHM, dark urine & jaundice.

Def: Donath - Lendsteiner reaction.

Chilling of blood sample → rewarming
in presence of "C" → Hemolysis.
↓
Complement

Diagnosis of Gummatosis (Bg Tertiary S)

- ①. CIP & Rad.
- ②. Histopathology
- ③. Serology (+ve)
- ④. CSF Exam ✓
- ⑤. CXR & Echo.

DM

Q: DGM For Gummatosis
lesion??

-ve



Very low no. of organisms ✓

Neuro §

H1

(Levin, et al)

P. 92

Icid: 8% of untreated § patients.

onset: 8-10 yrs after Inf.

NB: T. pallidum can be found in CSF

(4-24%) From time of chancre appearance. (CNS affect+
can occur in
any stage of §
even early)

Classification: T. pallidum may affect:

1. CSF → Asymptomatic Neuro §

2. Meninges → Meningeal Neuro §

3. B Vs → Vascular Neuro §

4. Parynchoma → Parynchomatous neuro §

① Asymptomatic Neuro §: (Latent Neuro §)

diag: AbnL CSF in absence of
Neurological S. & S.

+ve CSF changes ④

Most Sensitive
Indices & 1st
to return after good
th.

• Lymphocytes \geq 5/HPF

• Protein $>$ 40 mg/l. (IgG & IgM)

• +ve Serology For § $\left\{ \begin{array}{l} \text{specific} \\ \text{non specific} \end{array} \right.$ (in) $\left\{ \begin{array}{l} \text{Serum} \\ \text{CSF} \end{array} \right.$

↑
Globulins

• +ve Colloidal Gold test (Lange test):

in § The A/G ratio shows
predominance of G.

Colloidal Gold sol is $\left\{ \begin{array}{l} \text{ppt. by Globulins} \\ \text{protected from ppt.} \\ \text{by Albumin.} \end{array} \right.$

• Serial dilutions of CSF

($\frac{1}{10}$ - $\frac{1}{5120}$) + 4 ml Colloid Gold
sol.

→ Assess degree of ppt. From the
Color of the fluid:

Results

- 0-1 → NL
- 2-5 → AbNL

- ① → Red rose (No ppt)
- ② → reddish blue
- ③ → Lilac or purple (S. P-1)
- ④ → Blue
- ⑤ → Colorless, Trace of blue
- ⑥ → Colorless (Complete ppt)

NB This test reflects changes in CSF protein
& Not specific Test For S.

Classification of Asympt. Neuro S:

1. Type I

- Cell & protein changes → minimal
- Reagin tests → -ve
- Lange test → NL Curve.

2. Type II

- Cell & proteins → ↑
- Reagin tests → weak +ve
- Lange test → mid Zone

3. Type III

- Cell & protein → ↑
- Reagin → strong +ve
- Lange → 1st Zone Curve.

↓
بدرجته من سكريات
GPI 2)

Fate of Asymptomatic Neuro S: either

- ① Spontaneous resolution
- ② Progression To Symptomatic Neuro S. (this
Called Red Flag of Stokes) مقادير

Indications For CSF Exam:

- ① 2 yrs after # of Early S (to exclude Asympt. Neuro S)
- ② Serorepositive & relapse after # of Early S
- ③ if There are Neurological SXS
- ④ HIV patients. (High Incd of Neuro S).

در نتیجه عودت
بافت

Serology of
Relapsed
result.

Table 10.1: Classification

Asymptomatic	No signs/symptoms	CSF changes only
Meningeal	Cerebral	Acute, subacute or chronic meningitis affecting the vertex or the base of the brain
	Spinal	Hypertrophic cervical pachy-meningitis, doisolumbar meningitis and amyotrophic lateral sclerosis
Vascular	Cerebral	Syphilitic vascular thrombosis leading to various syndromes depending upon arteries involved.
	Spinal	Syphilitic vascular thrombosis leading to paraplegia below the level of involvement.
Parenchymatous	Cerebral	General paralysis of insane. Primary optic atrophy.
	Spinal	Tabes dorsalis.
Gumma	Cerebral	Symptoms and signs of space occupying lesion.
	Spinal	Symptoms and signs of space occupying lesion.

② Meningo-Vascular Neuro (Good prognosis if Treated Adequately).

Meningitis

Brain
(Cerebral)

Spinal Cord

End. arteritis

Brain Cord

- ICT
- Convulsion, Congestion & aphasia
- Cranial N. Paralysis ($\frac{2}{4}$ & $\frac{3}{4}$)
- Hydrocephalus
- Subependymal gliosis

"Argyll Robertson pupil"

- 4 - pin point
- 1 - irregular
- lost light reflex
- Preserved Accommodation

Cerebral Gumma

Cervical (8)
Myelitis

• UMNL:
at level 8.
Shoulder girdle.

• LMNL: below
level 8. lesion
(Erb's Spastic
Paraplegia)

• Amyotrophic L.S.

• Hypertrophic Cervical
Polyneuritis

• Ischemia
• Thrombosis &
• Gliosis

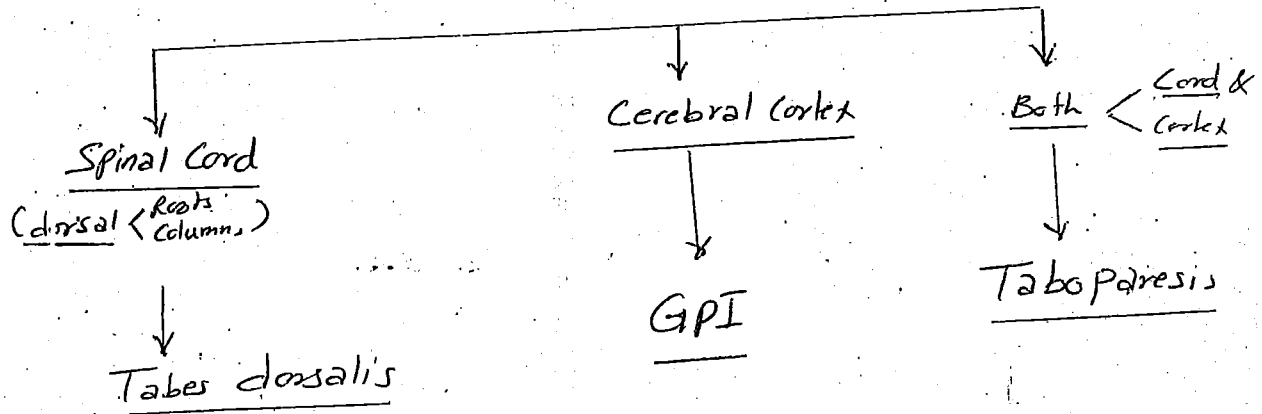
→ Spastic leg
Weakness
→ loss of sphincter
control.

"lat. sclerosis"

Parenchymatous Neurop

P. 95

§ of Parenchyma
may affect



Tabes Dorsalis

(Tabes = degen. or wasting)

wrinkled brow
Pseudo-ptosis
Argyll Robertson
optic atrophy
painless gastric ulcer
gastric crasis

Loss of pain
postural sense
temp. sense
vibration sense
deep reflexes
sensory loss in limbs

hype sensory loss
(Butterfly)

incontinence

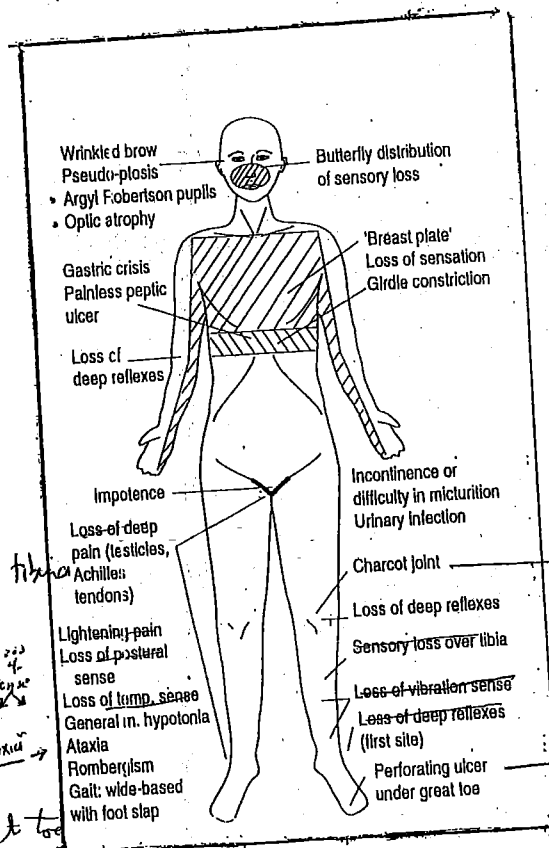
Ataxia

wide based gait

perforating ulcer under great toe

incontinence

Diagnosis



enlarged, no eff. 1
Hyper mobile, deformed
→ dislocate & EOS

Indolent, circular

painless

- Longe Test : G II (Lentic) Curve
- Reagin Test : 25% -ve
- FTAA BS : 90% +ve

General Paralysis of Insane (GPI)

P. 96

def progressive parenchymatous dis. of the brain

That produce

- ① physical & mental deterioration
- ② complete dementia.
- ③ Paralysis
- ④ Incontinence

"Hand writing"

onset : 10-20 yrs after Inf.

C/P :

Symptoms

- Intellectual impairment
- Failed memory
- ↓ Concentration
- ↓ Judgement
- Delusion
- Dementia
- Mood changes.

Signs

- Tremor of Tongue
Hands
- Abnl. pupils
- Dysarthria
- Convulsions
- Incontinence
- Pyramidal Signs

Pathology

- dura Matter → Thickened & adherent to skull
- pia Matter → " & " to cortex
- Mic. → Perivascular infilt. of Arterioles & meninges
- Iron containing Histiocytes (Microglia)

Pathognomonic

NB on GPI

P. 97

Exam of patient:

1. Mental status → deteriorated
2. Speech → dysarthria, hesitancy & slurring
3. Ocular (Pupil) Changes:

• Commonest sign in GPI

• Argyll Robertson pupil

4. Hand Writing:

• Misspelling & $\left\{ \begin{array}{l} \text{words} \\ \text{omissions} \end{array} \right.$

• Misplacements & repetitions of
Letters & Syllables.

(Agraphia) in Late stages

5. Face :

• Expressionless
• Flattening & smoothening
of nasolabial folds
• Tremors of lips &
Tongue.

انجمن طب و دندانپزشکی

Thomas Rodrigues
Aldome -airo Bardes
Goa

Thomas Rodrigues
Moura Bardes
Goa

Fig. 10.1: Handwriting of GPI

Diagnosis : Large Type III

- WR 100% +ve
- EEG +ve in 50%

Cardio Vascular § (CV §)

HL

عز الدين
(- ٢٠٠٦)
2006

P. 98

Incid: 8% of untreated §.

onset: 10-18 Ys.

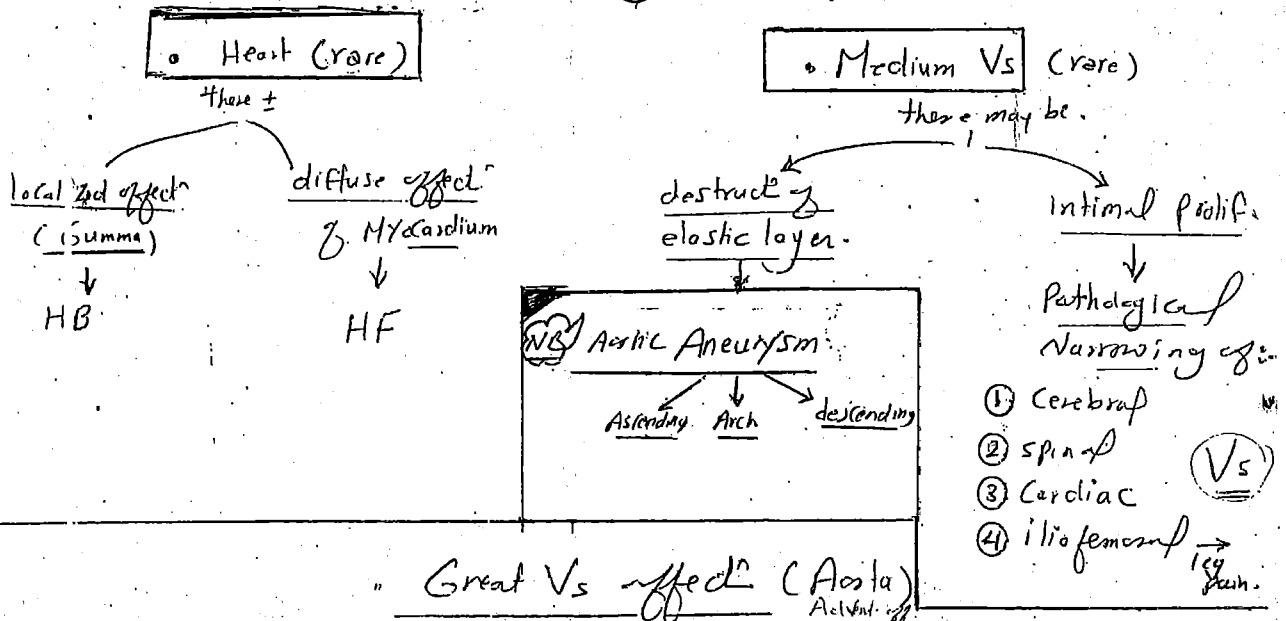
M:F = 1:3

40% are Neurop

Classification: it may affect:

- ① Heart
- ② Medium Vs Cerebral
Carotid
Hepatic
- ③ Great Vs. (Aorta)

legs.



the organism reach the (Vs) via Vasa Vasorum in the adventitia (where) it excites cellular infiltr. of plasma cells & Lymphocytes →:

- ① Adventitia: → fibrosis & narrowing of Vasa Vasorum
- ② Media: → fibrosis & destruction → Saccular aneurysm & ± AR (if extend to Aortic Ring)
- ③ Intima: → destruction, thickening & Calcificat patches → Coronary Atherosclerosis.

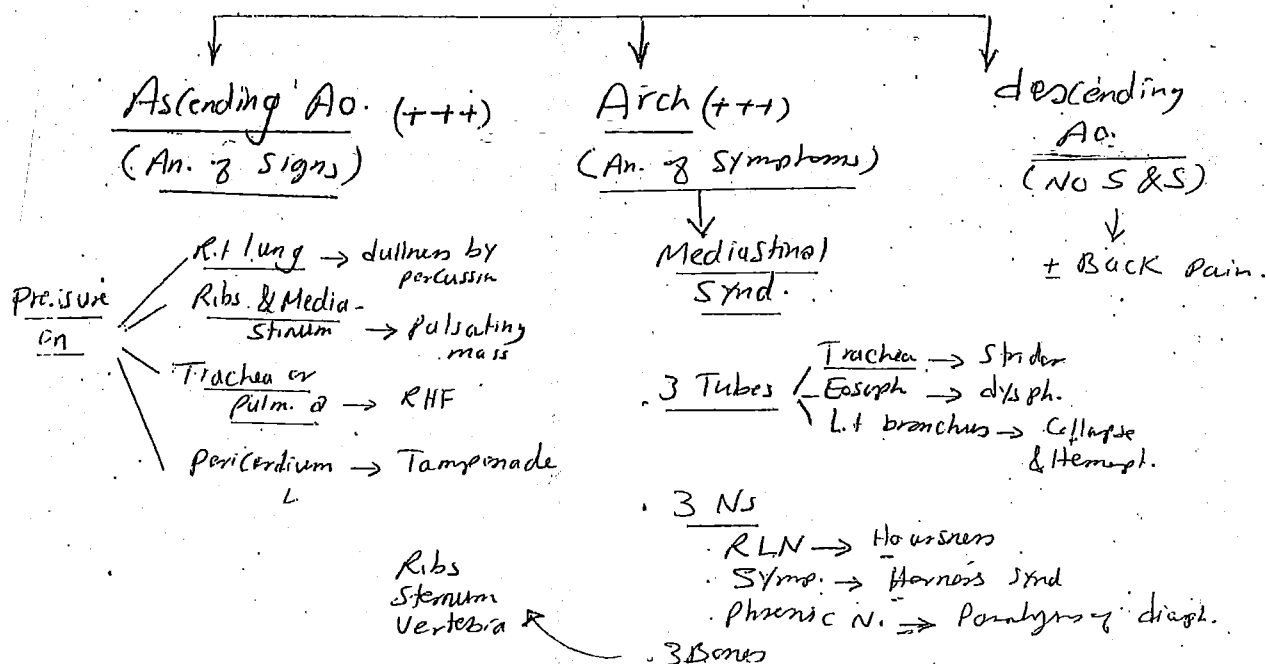
NB. Aneurysm of § is saccular while of Atherosclerosis is fusiform

CIP

usually Ascending

① uncomplicated Aortitis → Retrosternal pain or Asymptomatic.② AR → manif. of RHF. → "Commonest"③ Aortic Aneurysm
 Ascending: Aortic Systolic Murmur.
 Arch: → Mediastinal Synd
 descending → vertebral erosion & low back pain.④ Coronary ostial stenosis: Angina & death.Diagnosis

- ① CIP
- ② x Ray & Echo
- ③ Serology (+ve in 80%)
- ④ CSF (to exclude Neuro).

NB:Aortic Aneurysms

Congenital S (سعال اطفال) (prenatal S)

def Transplacental (Prenatal) Transmission of S
From Infected mother (usually during early S)
To the fetus (after the 4th month).

infection $\left\{ \begin{array}{l} \text{Early S (1st, 2nd \& Early latent)} \\ \text{after 4th month (T. pallidum can't cross the placenta except after 4th month).} \end{array} \right.$

العدوى السيلية transplacental

Note: Infection is Transplacental S
in contrast to Gonorrhea, Chlamydia & HSV
occurs Intrapartum (Vaginal delivery) $\xrightarrow{\text{So}}$ No 1st stage (Blood borne inf.)

S & pregnancy:

A - Effects of S on $\left\{ \begin{array}{l} \text{Pregnant Mother: Benign} \\ \text{Fetus} \end{array} \right.$ Same effect as in non-pregnant

- ① Abortion after the 4th m.
- ② prematurity
- ③ Still born (macerated fetus)
- ④ Cong. S either $\left\{ \begin{array}{l} \text{at time of delivery} \\ \text{NL then develop S. (usually 3wks-3m)} \end{array} \right.$
- ⑤ Healthy child
- ⑥ Placental S: placenta is bulky; Heavy, Greasy & pale & Large No of T. pallidum.

Hygic bullae (Large & TP)
Macerated
Protrudent
Abd + HLM

كل ما تلاحظه
كل ما تلاحظه
الجديد

→ ⑦ Kassowitz law: better prognosis occurs in successive pregnancies [d.t. Prolongation of period from the date of Maternal Inf.]

Risk of Infection:

- ن. ١١٢٢
- ① Conception \rightarrow Fth m \rightarrow loc. Transmission
 - ② 7 & 8 m \rightarrow \downarrow risk
 - ③ 3-6 wks before delivery \rightarrow No Transplacental Transmission but may be Intrapartum

B Effect of Infant on the mother:

(Colles Law): Infant doesn't Infect the mother who is already Infected & has a degree of Immunity.

3 Laws
Kassowitz
Profeta
Colles.

30891
Profeta law:

because the baby may be born healthy & then develop Syphilis after (ws - ms), So: one should depend on investigations of Blood Sample taken from umbilical Veins Acc. to "Profeta law".

(NB) Results of umbilical Vein sampling may be:

False - Ve (doesn't Exclude Inf.)

So Follow up for 3 ms For development & Later on.

False + Ve

d.t passive Transfer For Abs From The mother

So

look for VDRL Rising titer (Diagnostic) "الانف"

FTAAT (IgM)

(IgM doesn't cross the placenta)

[Inf. = ناتقل]

Good

good # 3 Mother

Before 4ms → Prevent Infect

after 4ms → In utero cure doesn't prevent

Bone joint

neural degres. IK.

affects

IK deafness (nerve) clutton's joint

→ (1) Hypersensitivity React

(Hydroarthrosis)

Long. &

• Late Cong. & not infectious

Stigmata of Cong.

- 2. Hypersensitivity manif.
- 3. Bones
- 4. Neuros
- 5. CV &
- 6. Blood

(Cochlear)
(Vestibular)
(Cochlear)
(Cochlear)

Definitely: similar to tertiary & (Gumma) + others

② Hypersensitivity manif: (3 hrs)

Interstitial Keratitis: the commonest lesion, its hyper sensitivity react that →

- Conjunctival vascularization: salmon patch
- Cellular infiltration: Ground glass (Hazziman)
- Cochlear neuritis: Cochlear nerve inflamm.

③ CV & Rare

④ Blood: Paroxysmal Cold haemoglobinuria (PCH)

→ perceptive deafness

N.B: Conductive deafness may occur d.t. & Rhinitis

in early stage of Cong. &

Clotting or Thrombosis: Painless effusion of knee joint

(little) impairment of Mobility

Rad: enlarged joint spaces (no bone)

or Cartilage changes

At first: Bone formed

Later on: Bone destroyed

Clavicle: "Hinge" joint

Tibia: "Saber" tibia

Nasal Septum destroyed

Palate perforated

in 2 yrs infectious "usually no 1st stage but (Chancres)" Blood born inf) but (Chancres) may occur from sexually infected mother during Vaginal delivery

on xcha placenta Perforated Fractures

④ Neuros: as in adult

⑤ CV & Rare

⑥ Blood: Paroxysmal Cold haemoglobinuria (PCH)

⑦ Bone: At first: Bone formed

Later on: Bone destroyed

Clavicle: "Hinge" joint

Tibia: "Saber" tibia

Nasal Septum destroyed

Palate perforated

• Early Cong. & (Similar to 2nd Acq. &)

A Rash as before + Bullous pp. Eruption (earliest Erupts = & pemphigus) (+)

B Generalized L.N

C Mucous patches → Rhinitis & Stiffness → Conductive deafness

D General Manifests:

① Senile facies: d.t. dehydration (Wrinkled face + CAL color & skin)

② CNS: Syphilitic Meningitis → Stiffness Pulsing fontanelle

③ CVS: "very" rare

④ RS: may be fetal pneumonia

⑤ Renal: NS or Acute Nephritis

⑥ Lymphatic syst: HSM & L.N & LCF

10

(نقص) Stigmata (Remainders) of Cong.

Syphilis

(Permanent scars & deformities that result from the lesions of Cong. & persist for life)

Stigmata of Early (8) (40%)

Lesions

1. Salt & Pepper fundus (Residual areas of pig. & atrophy)
2. Saddle Nose: depressed nasal bridge

3. High arched Palate: (dit improper development of Maxilla.)

4. Bulldog face: short maxillae + Frontal bossing (vis) of Skull.

5. Rhagades: linear scars at angles of Mouth.

6. Hutchinson teeth: (improper teeth development) Teeth Ch. By:

- Widely spaced
- Shorter than Lat. Incisors
- Thick in ant. post. diameters
- Screw driver appearance:
- Notched (dit effect of Trauma)

Cutina ends narrower than the gingival ends.

7. Moon's Molars (Mull berry Molars):

usually at 1st lower Molar; 4 Cuops are packed Together in The center Instead of being at Corners
→ Some shaped teeth with wider gingival Margin Than The Cutting ends.

8. Onychia

+ Hutchinson Triad

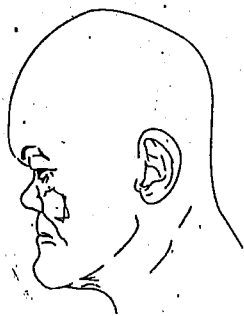
Ch. By Δ of:

- Perceptive deafness
- Hutchinson Teeth
- IK

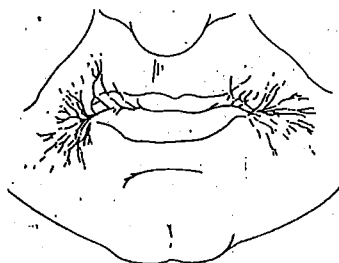
Stigmata of Late (6) Lesions

- Corneal Opacity (IK)
- Optic atrophy
- Perceptive deafness (8th Nerve)
- Sabre tibia (Bowling of ant. Tibia)
- Frontal bossing of Skull (Olympian Brow)
- Perforating nasal Septum or Soft Palate.

Ghost vis. Filming IK (stock & faces)



Bulldog face with saddle nose and relative prominence of lower jaw in late congenital \$



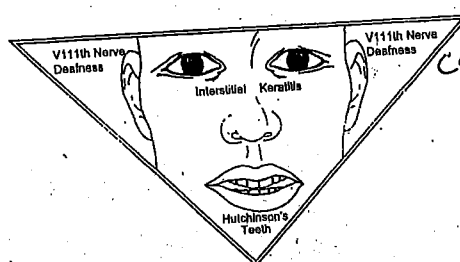
Scars at angles of mouth (rhagades) are stigmata of congenital syphilis



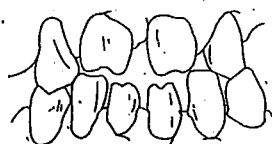
Gummatous destruction of the nasal septum and collapsed lower part of nose in late congenital \$



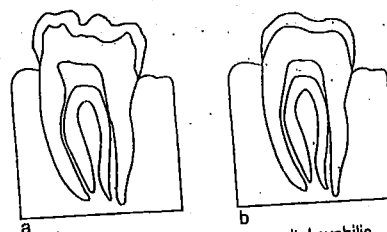
Clinical appearance of sabre tibia in late congenital \$



Hutchinson's triad in late congenital \$



Hutchinson's incisors in late congenital \$



Moon's molars in late congenital syphilis (a) normal (b) abnormal

Diagnosis of Cong S

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- ① CIP & Stigmata
- ② Radiological Bone Exam.
- ③ DGM: From $\left\{ \begin{array}{l} \text{MM lesions} \\ \text{umbilical vein} \\ \text{nasal secretions} \end{array} \right.$

④ Serological testing (See profeta law):

if false +ve

عشان نعرف شوية

لغة
Semi Arabic

في
(عنوان استبيان)

either ① Rising titer (VDRL)

② FTA-ABS test: using Fluorescein labelled IgM conjugate.

(Not The usual Fluorescein labelled Antihuman globulin)

Neonatal pustular eruptions

1. Infantile acne.
 2. Impetigo.
 3. Congenital S.
 4. Neonatal listeriosis.
 5. TS.
 6. Neonatal candidiasis ①
 7. Malassezia furfur.
 8. Scabies.
 9. Miliaria.
 10. Eosinophilic pustulosis.
 11. Toxic erythema neonatorum ②
 12. Infantile acropustulosis.
 13. Transient neonatal pustulosis ③
 14. Pustular psoriasis ④
- see also chapter 21, p. 108.

↓
Because IgM can't cross the placenta so diagnostic of +ve in fetus.

↓
But False -ve results may occur if "spill over" IgM from The mother occurs at placental degeneration

عشان
→ Assess ceruloplasmin level.

• In pregnant → double level of non pregnant Adult.

• In Infants → half NL Adult

So: Compare 2 concentrations to detect if leakage have occurred or not (leakage of IgM from mother to Fetus)

في
Rising titre of VDRL

Serological Tests For S

Non-specific Tests

(non Treponemal tests)

Reagin tests

simple
cheap
good
follow up

wait
min

②

Flocculation tests

CFT

①. VDRL

venereal dis.
Research
Laboratory
test

②. RPR

③. Automated reagin Tests (ART)

* these tests are non specific
a. they depend on the use
on antigen other than T. Pallidum

Thus Antigen Called: "Cardiolipin" is

is an alcoholic extract of beef
heart muscle & has the ability
to react with a ^{specific} gamma globulin
Present in the Patient's Serum Called

"Reagin"

(Ag) → Cardiolipin + (Ab) Reagin → ^{Visible} Reaction

the reagin is present in very small
amount in all NL sera but in large
amounts in sera of syphilitic patients.
to the degree that when react with the
cardiolipin can produce visible reaction (either)

rough flocculation
or
complement fixation

Specific Tests

(Treponemal tests)

TPHA

TPIT (Treponemal P. immn reaction)

FTA Fluorescent test

FTA Abs.

RP-CFT

RPR (Rapid Plasma Reagin) - complement test

these tests are

specific as they depend
on detection of treponemal
Antigens. So named
(Treponemal tests)

Fluorescent
Treponemal
Ab titre

non
pathogenic
Treponema

Adv. they are accurate
don't give false results
So used as confirmatory
for non specific tests.

Disadv:

- ①. expensive
- ②. Technically difficult
- ③. Remains +ve for life,
So can't be used
for follow up of the
Results.

TPHA

rabbit TP Ag

US rabbit

RBCs

TP

- not turn -ve
→ once +ve → +ve forever

Non Specific Tests

P. 108

Advantages:
"w" (w) (Specific)

- ① easy
- ② cheap
- ③ Sensitive (so screening; good -ve tests).
- ④ Can be used to follow up the Ht results as they are become -ve after effective Ht specially if quantitative estimation of their titer is used (Serial quantitative VDRL)

used for
Screening (Sensitive - Good -ve)
Follow up of Ht results

Disadv. they may be false +ve or false -ve (So) (non specific) should be confirmed with one of the specific tests.

False +ve

- ① Technical faults
- ② pregnancy
- ③ old age
- ④ Idiopathic
- ⑤ BFP: conditions ch by Liberator of large amounts of Cardiolipin from organisms other than Treponema

No cell d.t. Cellular destruction as:
Ab against

- a. Viral pneumonia
- b. Malaria
- c. Hepatitis *
- d. Measles, Mumps.
- e. Chicken pox.
- f. Vaccinal
- g. Treponema (dis) other than

I Acute Condition
(Reaction +ve For ≤ 6 ms)

II Chronic Condition

(Reaction remains +ve > 6 ms)

- a. SLE
- b. Rheum
- c. Anemia
- d. Leprosy (LL > TL)
- e. Mg
- f. Sarcoidosis

if reactive False +ve \rightarrow titre

False -ve (d.t.)

1 Prozone phenomenon

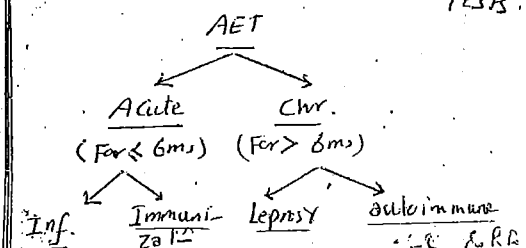
Failure of occurrence of Flocculation reaction d.t. high conc. of Abs in Patients Serum except after serial dilution.
(only with Flocculation tests Not with CFT)

2. Mg

3. HIV

Biological False +ve (BFP)

patient is No Hx or clinical data of $\&$ with $\begin{cases} +ve: \text{non specific tests} \\ -ve: \text{specific tests} \end{cases}$



Flocculation tests: $\left\{ \begin{array}{l} \text{VDRL} \\ \text{RPR} \end{array} \right.$

VDRL
RPR

Cardiolipin Ag + Small amount
of pt. serum \rightarrow Flocculated
that can be detected by NE or MIC.

((المستعمل هو VDRL))

CFT (WR): (لاين)

Cardiolipin + Serum + C Addition \rightarrow
mix \rightarrow add sensitized sheep RBCs
(RBCs Coated with Anti RBCs) \rightarrow Ab
if (-ve) hemolysis \rightarrow (+ve) test (S)
if (+ve) Hemolysis \rightarrow (-ve) test (Not S)

X. ART: VDRL is auto-analyzer to perform Ag. How??

Specific tests (المستعمل هو تريبونيم) (other virulent strains)

المستعمل هو

① TPHA:

2 tubes.

Test tube

Control tube

Sensitized sheep RBCs
(Treponema Coated sheep RBCs)
+
pt. Serum.

Non sensitized sheep RBCs
+
Patient Serum.

Test is +ve if there is
agglutination in (test) tube
"only".

أستعمل اختبار... وهو المستعمل حالياً
في مصر

② TPI: Serum + Treponema + C⁺ Addition

DGM Exam. → Immobilization of Treponema.

- disadv. ① difficult
② delayed result till end of 1st year.

③ FTA: Serum + Treponemae (dead) → Treponemal Coating by test

Abs: to detect this coating add Conjugate

[Fluorescein labelled Anti human Igs] →

Fluorescein under MIC.

④ FTAA: as FTA but before doing it, the Serum is diluted by culture extract of other

Treponemae to Absorb non specific Abs.

"Reiter"

against other Treponemas →

So no false +ve results

Adv ① No false +ve results.

② the only test that's +ve in early phase of Iry & (2nd w)

③ used to dx Cong. & ^{More} specifically "why?"

• because: this test can be done by using specific class of Conjugate (IgM), since IgM don't cross the placenta, a reactive test in infant specifically indicates Cong. &

However: frequent determination of Rising titer of VDRL

is more easy & cheap (because FTAA sensitivity is < 90% in 1st month & < 60% after 15 " so VDRL is Better)



if very early Iry
(revert to -ve)

2 Standard tests for Cong. &

2 Standard tests for Cong. &

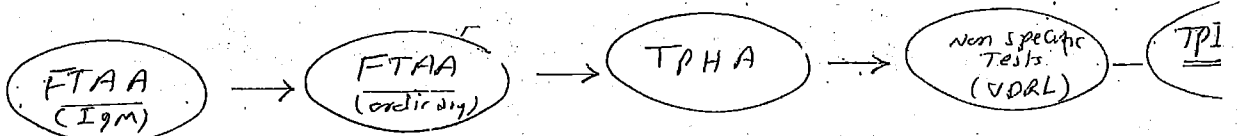
⑤ Reiter protein CFT: the Ag is protein derived from Reiter strain of Treponema that's antigenically similar to T. pallidum + Patient serum in presence of Complement

NB: on Serological Tests

- A. onset of positivity.
- B. duration of "
- C. % of positivity in each stage.

A. onset of positivity:

FTAA (IgM) → end of 2nd w.
 FTAA (ordinary) → during 3rd w.
 TPHA → " " "
 Non specific tests → 3-4 wks after Inf. (1-2 wks after appearance of chancre)
 TPI → after end of 2nd stage (> 12 wks)



- ① Neonatal & (But False +ve (10%) : in placental degeneration)
False -ve (30%) : after 1st m.; ↓ Sensitivity
- ② Very Early Diagnosis of chancre (when DGM is -ve)
- ③ ± Follow up

So it's the Most Sensitive in 1st Stage.

B. Duration of Positivity: see below.

سوال
کے جواب

How long do serological tests For Φ remain +ve??

[A] Non specific serological tests \rightarrow All remains +ve
Except after HT.

if HT started \rightarrow Before +ve tests ($< 3-4$ wks) \rightarrow No Sero +ve & pt. remains Sero -ve
after +ve tests (in 1ry & 2ry stages) \rightarrow Sero -ve after 3-6 m From Initiation of HT
in Latent & Late Φ : progressive slow \downarrow in Sero +ve till become Sero (-ve)
Except: Some cases remains with Fixed titer (Sero fast \odot W-R Fast)

[B] Specific serological tests: all remains +ve For life
(Even \bar{e} HT). Except FTAA (IgM) $\downarrow \downarrow$ in months
(Specially \bar{e} HT)

\rightarrow (So it is) the only specific tool
That can be used to
Follow up of HT

نکات
یاد رکھو $\left\{ \begin{array}{l} \text{Non specific tests: Their Titer } \downarrow \text{ with HT EXCEPT Sero fast condition} \\ \text{Specific tests: once +ve, always +ve EXCEPT FTAA (IgM)} \end{array} \right.$
(خاصیتوں کے ساتھ ساتھ)

[C] HT positivity:

1ry stage \rightarrow 50% +ve
2ry " \rightarrow 100% +ve (EXCEPT \bar{e})
late Φ \rightarrow Most +ve \bar{e} EXCEPT
FTAA (IgM).

Treatment of S

P. 113

BASIC principles:

- ① Penicillin G \rightarrow 1st choice
- ② Treponema multiply 130 hrs & this requires Treponemidal level in tissues for at least 8ds.
- ③ Any organ can be affected by T. pallidum including the brain & this require drug that can cross the BBB.

So Procaine penicillin & Crystalline P.

$\xrightarrow{\text{Benzathine}}$ Benzathine Penicillin. (as they can cross BBB)
 (lipid insoluble, can't pass BBB)

IVB. Types of Penicillin:

- ① Crystalline Penicillin (1 million U / amp) $\left\{ \begin{array}{l} \text{IM} \\ \text{or} \\ \text{IV} \end{array} \right.$
- ② Procaine Penicillin (600,000 U / amp) \rightarrow IM only
- ③ Benzathine Penicillin (1.2 MU / amp) \rightarrow IM only
 \downarrow don't pass BBB

Note: Benzathine P \rightarrow Compliance
 Procain & Crystalline P. \rightarrow (BBB) use for Neuro S

Treatment ① (Probenecid) ② C

Early S (< 2y)

Late S (> 2y)

(Gumma & CV S)

- ① Procaine P (أسيول عضلي) 600,000
② Benzathine P (أسيول طويل المفعول حبة واحدة) 2,4 M

- ① Procaine P
② Benzathine P
أسيول عضلي كل أسبوع
لثلاثة أسابيع

Neuro S
&
ocular S

① علاج لثلاثة أسابيع

من
Crystalline P أو Procaine P
أسيول عضلي
كل أسبوعين
أو
أسيول طويل المفعول حبة واحدة

Amoxycillin
[6 gm 1d for 20ds.]

Ceftriaxone 2gm IM or IV for 20ds daily.

Neonatal Syphilis: Neonate with:

Proven or highly probable or
as mother with untreated
Early S
(أ. أ. أ. ح.)

Procaine 50,000 U/kg 1d x 10ds
Crystalline (IV) < 7ds 50,000 U/kg x 2 1d IV
3ds " x 3 1d IV [100-150,000 U/kg 1d IV]

No signs of dis. or
born to mother &
Treated S → Benzathine

50,000 U/kg
أسيول عضلي حبة واحدة
(Benzathine)

NB

- in All Penicillin Ht
Cases: Give 1gm
probenecid 1day
before penicillin Inj.
Why?
① ↓ renal Exc. → ↑ plasma P.
② displacement of P.
from plasma protein
→ level
Except
in Ht of Neuro S
why
① may Ht with Pn
distribution of P.
in brain
② ↑ Adverse reac.

Treatment in other situations

① Pregnant: as in non pregnant Adult

if there is penicillin Allergy →

Azithromycin or Erythromycin or Ceftriaxone

• VDRL: done quantitatively free delivery to detect any clinical or serological relapse.

No tetracycline

② The following treated as Neurosy: < ^{ocular} HIV

⊠ HIV (See) (dr High Incid. of Neurosy)

⊠ Optic atrophy or Nerve deafness (Add Cs)

Amoxycillin

⊠ IK ?

(add 0.5 prednisolone EDs or Atropine EDs)

eye doctor

③ In cases of penicillin allergy:

✓ Tetracycline HCl. 2gm daily

✓ Doxycycline : 200 mg "

✓ Erythromycin : 2gm daily

for { 15 ds : in Early stage
30 ds : Late stage

NB: • Azithromycin may be used:

• Early sy → 2gm Single dose

• Pregnant → 1gm 1st, 2nd, 3rd, 4th, 5th, 6th, 7th, 8th, 9th, 10th (10-)

• Ceftriaxone:

also → Early sy → 1gm 1d for 1w.

Pregnant • Neurosy → 2gm 1d " 20ds

توصيات علاجية ...

Tetra
Doxycy
Ceftria

15 ds
30 ds

Erythro
Azithro
Ceftriaxone

Amoxycillin

• Follow up of S Patient: BY (VDRL).

1. 1, 3, 6, 12 months after $\#$

For $\left\{ \begin{array}{l} \text{upto 2y: in Early S} \\ \text{upto 3y: in Late S} \end{array} \right.$

2. Neuro S or AbNL CSF: CSF exam / 6 months

FIPP $\left\{ \begin{array}{l} \text{NL cell counts} \\ \text{-ve CSF VDRL} \end{array} \right.$

• ReTreatment if:

① Clinical relapse \rightarrow persistent or recurrent S & S

② Serologica \rightarrow Sustained 4 Fold \uparrow in VDRL
 \rightarrow Failed \downarrow in VDRL < 4 Fold
 in 1 yr after $\#$.
 (treat as late S)

vp. ag Reaction to $\#$

① Penicillin Reactions:

② Immediate $\left\{ \begin{array}{l} \text{Urticaria} \\ \text{Angioedema} \\ \text{Anaphylactic shock} \end{array} \right.$

lie down & Feet raised.

air way

$\#$ $\left\{ \begin{array}{l} \text{adrenaline } 1/1000 \text{ 0.5 ml IM (In)} \end{array} \right.$

Hydrocortisone 250 mg IM

Aminophylline 250 mg IM

③ delayed: 1-2 wks. CIP $\left\{ \begin{array}{l} \text{Serum sickness like} \\ \text{skin Rash} \end{array} \right.$

Fever, arthralgia

proteinuria \times EN

$\#$ anti histamines.

② Procaine Reaction: (Hoigne's reaction):

d.t Procaine Fract (\pm occur \bar{e} $<$ Benzathine & Amoxycillin.)

• Acute Non Allergic Psychiatric React

• Tachycardia

• Confusion

• Cyanosis

• Hallucinations

$\#$ No $\#$, Spont $\downarrow \downarrow$
 \bar{e} in 1 hr.

③ Janisch-Herxheimer Reaction: ~ [100]

AET: Allergic reaction (Not drug reaction)
That occurs with the First dose of
Antisymphilic # (Penicillin).

Fuller add or
None Rule

لور و جرس: جرس (لا. ٤)

Mech. anti $\&$ H may \rightarrow

- ① released Treponemal endotoxins
- or ② Antibodies format after rapid release of Treponemal Ags.

onset: 3-12 hr after 1st injected dose.

3-12 hr after

CIP

Early $\&$ (More common)

affect (50%) of pts.

usually: Mild

CIP ① FAHM

② Inflamm. of preexisting $\&$ lesions:

- Chancre
- L-N
- Skin Rash

① Prevention

② Active H \rightarrow Cs.

Late $\&$ (More dangerous)

affect (25%) of pts.

may be mild (Fever)
or dangerous

- ① in $\&$ Aortitis \rightarrow Coronary occlusion
- ② in $\&$ Laryngitis \rightarrow suppurat.
- ③ GPI \rightarrow Convulsion

(٤ علا. ١٠٠)

فرض هویت که رسم آیتوم قبل لیلاج
در طه یومیه بعد لیلاج و لیلاج
تدریجاً

④ Therapeutic paradox: worsening of the dis.
after tt d.t. Excessive scarring
produced by too rapid destruction of
Treponemas

More in patients with Aortic dis

⑤ Vaso Vagal attack: Lying down & elevated legs.

HIV & S:

S & other STDs that produce genital ulcers
Further ↑ risk of HIV Acquiring d.t

① Lack of epithelial barrier d.t ulcerate

② large No of Macrophages &
CD4 that Express HIV receptors.

③ Treponema ++ Macrophages → Cytokines.

S In HIV Patient ch By

① ↑ Incid of ulceration in 2nd lesion.

② ↑ Incid. of Bact. effects of Chancre → Painful chancre

③ ↑ " " Neuro S.

④ Serology may be $\begin{cases} \text{very high} \\ \text{Low} \\ \text{Non Reactive} \end{cases}$

Done BY Biopsy.

⑤ H → Wt ↑

del
Treat as Neuro S
(C. S. F. no)

Wt ↓

+ CSF → Treat as Neuro
- CSF → " as Late
C. S. F. no

SEXUALLY TRANSMITTED AND TRANSMISSIBLE PATHOGENS

Bacteria

- ✓ *Neisseria gonorrhoeae*
- ✓ *Treponema pallidum*
- ✓ *Haemophilus ducreyi*
- ✓ *Chlamydia trachomatis*
- ✓ *Mycoplasma hominis*, *M. genitalium*
- ✓ *Ureaplasma urealyticum*
- ✓ *Gardnerella vaginalis*
- ✓ *Mobiluncus curtisii*, *M. mulieris*
- ✓ *Calymmatobacterium* (*Klebsiella*) *granulomatis*
- ✓ *Shigella* spp.
- ✓ *Campylobacter* spp.
- ✓ *Helicobacter cinaedi*, *H. fennelliae*

Virus

- ✓ Human immunodeficiency virus, types 1 and 2
- ✓ Herpes simplex virus, types 2 > 1
- ✓ Human papillomavirus
- ✓ Hepatitis viruses, B > C and (via fecal-oral contact) A
- ✓ Cytomegalovirus
- ✓ Molluscum contagiosum virus
- ✓ Human T-cell lymphotropic virus, types I and II
- ✓ Human herpes virus, type 8

Protozoa

- ✓ *Trichomonas vaginalis*
- ✓ *Entamoeba histolytica*
- ✓ *Giardia lamblia*

Fungi

- ✓ *Candida albicans*

Ectoparasites

- ✓ *Phthirus pubis*
- ✓ *Sarcoptes scabiei*

Table 31.1 Sexually transmitted and transmissible pathogens.

CEB